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 alerts (SDIs) affected
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 alerts (SDIs) affected
 NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness
 alerts (SDIs) affected
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 February 2005
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 (ROSPATENT) added to list of core patent offices covered
 NEWS 18 FEB 10 STN Patent Forums to be held in March 2005
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 National Meeting on March 13, 2005
 NEWS 20 FEB 28 PATDPAFULL - New display fields provide for legal status
 data from INPADOC
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 NEWS 22 FEB 28 MEDLINE/LMEDLINE reloaded
 NEWS 23 MAR 02 GBFULL: New full-text patent database on STN
 NEWS 24 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
 AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:44:41 ON 03 MAR 2005

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 14:44:50 ON 03 MAR 2005

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STRUCTURE FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

DICTIONARY FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

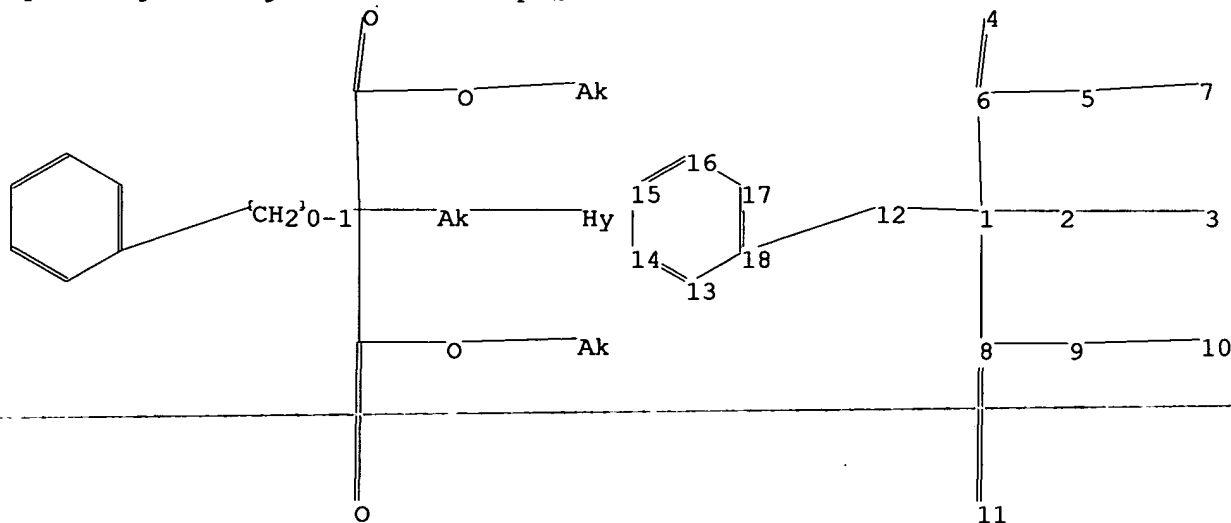
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\09854694.str



chain nodes :

1 2 3 4 5 6 7 8 9 10 11 12

ring nodes :

13 14 15 16 17 18

chain bonds :

1-2 1-6 1-8 1-12 2-3 4-6 5-6 5-7 8-9 8-11 9-10 12-18

ring bonds :

13-14 13-18 14-15 15-16 16-17 17-18
 exact/norm bonds :
 1-2 2-3 4-6 5-6 5-7 8-9 8-11 9-10
 exact bonds :
 1-6 1-8 1-12 12-18
 normalized bonds :
 13-14 13-18 14-15 15-16 16-17 17-18

Match level :

1:CLASS 2:CLASS 3:Atom 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
 10:CLASS 11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom
 Generic attributes :

3:

Saturation : Unsaturated

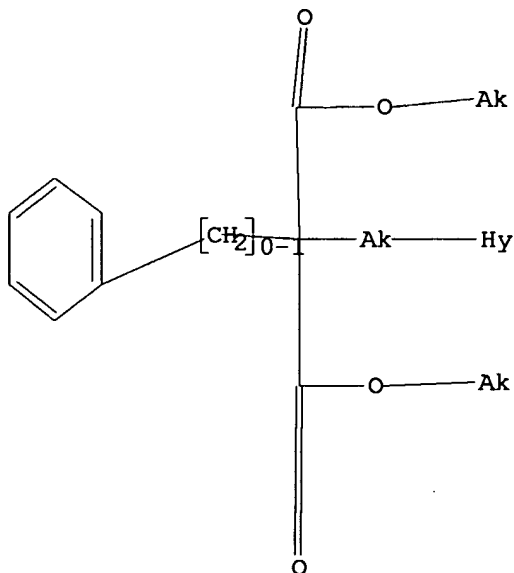
L1 STRUCTURE UPLOADED

=> dis l1

L1 HAS NO ANSWERS

L1

STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sam

SAMPLE SEARCH INITIATED 14:45:15 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 9934 TO ITERATE

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

09/854,694

BATCH **COMPLETE**

PROJECTED ITERATIONS: 192708 TO 204652
PROJECTED ANSWERS: 130 TO 664

L2 2 SEA SSS SAM L1

=> s 11 full

FULL SEARCH INITIATED 14:45:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 192928 TO ITERATE

100.0% PROCESSED 192928 ITERATIONS
SEARCH TIME: 00.00.12

201 ANSWERS

L3 201 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 161.33 | 161.54 |

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 14:45:41 ON 03 MAR 2005
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FILE COVERS 1907 - 3 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 2 Mar 2005 (20050302/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L4 96 L3

=> s 14 and pd<dec 1998

~~18918148 PD<DEC 1998~~

(PD<19981200)

L5 79 L4 AND PD<DEC 1998

=> dis 15 1-79 bib abs hitstr

L5 ANSWER 1 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

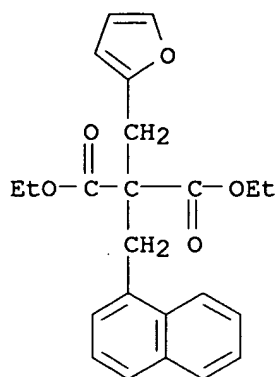
AN 1999:104651 CAPLUS

DN 130:139217

TI New synthesis of diethyl (1-naphthylmethyl)tetrahydrofurfurylmalonate

AU Zhou, Zhi-Ming; Chen, Nan

CS College of Chemical Engineering & Material Science, Beijing Institute of Technology, Beijing, 100081, Peop. Rep. China
 SO Gaodeng Xuexiao Huaxue Xuebao (1998), 19(12), 1979-1981
 CODEN: KTHPDM; ISSN: 0251-0790
 PB Gaodeng Jiaoyu Chubanshe
 DT Journal
 LA Chinese
 AB The title compound was prepared in 3 steps from furfural and di-Et malonate via alkylation of di-Et tetrahydrofurfurylmalonate with 1-(chloromethyl)naphthalene in DMF in the presence of NaH.
 IT **95432-29-4P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of di-Et (1-naphthylmethyl)tetrahydrofurfurylmalonate)
 RN 95432-29-4 CAPLUS
 CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 2 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1998:492785 CAPLUS
 DN 129:227381
 TI Specificity of pyridinium inhibitors of the ubiquinone reduction sites in mitochondrial complex I
 AU Miyoshi, Hideto; Iwata, Jun; Sakamoto, Kimitoshi; Furukawa, Hiroshi; Takada, Motoyuki; Iwamura, Hajime; Watanabe, Takashi; Kodama, Yoshio
 CS Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Kyoto, 606-8502, Japan
 SO Journal of Biological Chemistry (1998), 273(28), 17368-17374
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 OS CASREACT 129:227381
 AB Dual binding sites for pyridinium-type inhibitors in bovine heart mitochondrial complex I have been proposed (Gluck, M. R., Krueger, M. J., Ramsay, R. R., Sablin, S. O., Singer, T. P., and Nicklas, W. J. (1994) J. Biol. Chemical 269, 3167-3174). The marked biphasic nature of the dose-response curve for inhibition of the enzyme by MP-6(N-methyl-4-[2-(p-tert-butylbenzyl)propyl]-pyridinium) makes this compound the first selective inhibitor of the two sites (Miyoshi, H., Inoue, M., Okamoto, S., Ohshima, M., Sakamoto, K., and Iwamura, H. (1997) J. Biol. Chemical 272, 16176-16183). Modifications of the structure of MP-6 show that a tert-Bu group on the

benzene ring, a Me group attached to the pyridine nitrogen atom, para-substitution pattern in the pyridine ring, and the presence of a branched structure in the spacer moiety are important for the selective inhibition. On the basis of the structural specificity, we synthesized a selective inhibitor, MP-24 (N-methyl-4-[2-methyl-2-(p-tert-butylbenzyl)propyl]pyridinium), which elicits greater selectivity. Characterization of the inhibitory behavior of MP-24 provided further strong evidence for the dual binding sites model.

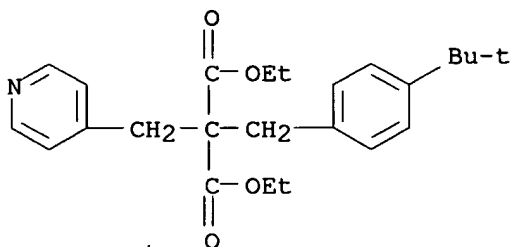
IT **212787-47-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridinium inhibitors of ubiquinone reduction sites in mitochondrial complex I)

RN 212787-47-8 CAPLUS

CN Propanedioic acid, [[4-(1,1-dimethylethyl)phenyl]methyl](4-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:686572 CAPLUS

DN 128:22692

TI Potential GABAB receptor antagonists. X. The synthesis of further analogs of baclofen, phaclofen and saclofen

AU Prager, Rolf H.; Schafer, Karl

CS Department of Chemistry, Flinders University of South Australia, Adelaide, S.A. 5001, Australia

SO Australian Journal of Chemistry (1997), 50(8), 813-823

CODEN: AJCHAS; ISSN: 0004-9425

PB CSIRO

DT Journal

LA English

AB In an attempt to obtain new compds. with binding activity at the GABAB receptor site, 3-amino-2-arylpropanoic acids and their sulfonic, phosphonic, and hydroxamic acid analogs were prepared. In addition, the isomer of phaclofen, 3-amino-1-(4-chlorophenyl)-propylphosphonic acid, and the higher homolog of baclofen, 5-amino-2-(4-chlorophenyl)pentanoic acid were prepared.

IT **112864-34-3P 199436-87-8P**

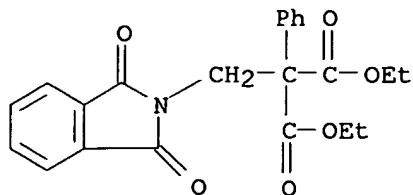
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and GABA receptor antagonist activity of baclofen, phaclofen, and saclofen analogs)

RN 112864-34-3 CAPLUS

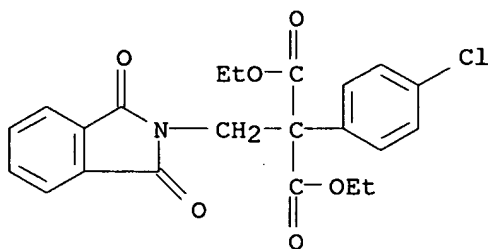
CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-

, diethyl ester (9CI) (CA INDEX NAME)



RN 199436-87-8 CAPLUS

CN Propanedioic acid, (4-chlorophenyl)[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:204398 CAPLUS

DN 126:264353

TI Preparation of acylated amino acids as endothelin antagonists

IN Doherty, Annette M.; Hamilton, Harriet W.; Kaltenbronn, James S.; Quin, Iii John

PA Warner-Lambert Company, USA

SO U.S., 16 pp.

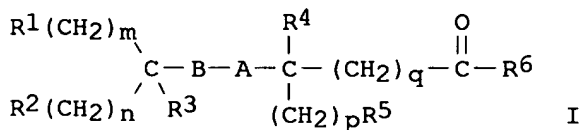
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|------|----------|-----------------|--------------|
| PI | US 5610177 | A | 19970311 | US 1994-287369 | 19940808 <-- |
| PRAT | US 1994-287389 | | 19940808 | | |
| OS | MARPAT 126:264353 | | | | |
| GI | | | | | |



AB Novel acylated amino acids I [R1, R2 = independently partially or completely unsatd., (un)substituted aryl or heteroaryl, (un)substituted C3-5 cycloalkyl; m, n = independently 1-3; R3 = H, straight or branched C1-4 alkyl; B = CH:CH, (CH2)r, r = 0-3; A = CONH, NHCO, CH2NH, CSNH, COCH2, CONMe, NMeCO; R4 = straight or branched C1-4 alkyl or C2-4 alkenyl, benzyl substituted with 0-3 halo, alkoxy, or alkyl groups; p = 0-3; R5 = partially or completely unsatd., (un)substituted aryl or heteroaryl; q = 0-3; R6 = OR7, NR8R9; R7 = H, lower alkyl; R8, R9 = independently H, lower alkyl; NR8R9 = 3-7 membered heterocyclic ring containing not more than 2 hetero atoms, and where the heteroatoms are separated by 2 carbon atoms] which are antagonists of endothelin are described. Methods for their preparation and pharmaceutical compns. containing them are also included. Compds. I are expected to be useful in treating elevated levels of endothelin, acute and chronic renal failure, hypertension, myocardial infarction, myocardial ischemia, cerebral vasospasm, cirrhosis, septic shock, congestive heart failure, endotoxic shock, subarachnoid hemorrhage, arrhythmias, asthma, preeclampsia, atherosclerotic disorders including Raynaud's disease and restenosis, angina, cancer, pulmonary hypertension, ischemic disease, gastric mucosal damage, hemorrhagic shock, ischemic bowel disease, diabetes, head injury, and stroke. Thus, acylation of α -methyl-D-tryptophan Me ester with bis(1-naphthylmethyl)acetyl chloride, followed by saponification with LiOH, gave acyltryptophan derivative (1-C10H7CH2)2CHCO- α -Me-D-Trp-OH (II). II and 15 related N-acyl- α -methylamino acid derivs. showed in vitro inhibition of endothelin-3 (ET-3)-stimulated arachidonic acid release in cultured Chinese hamster ovary cells.

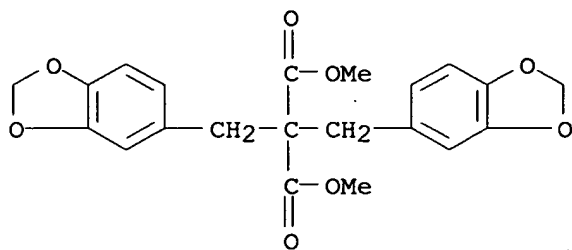
IT **188822-02-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acylated amino acids as endothelin antagonists)

RN 188822-02-8 CAPLUS

CN Propanedioic acid, bis(1,3-benzodioxol-5-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:70350 CAPLUS

DN 126:199453

TI Preparation of adamantyl indolylalkylcarbamates and analogs as cholecystokinin antagonists

IN Horwell, David C.; Roberts, Edward; Holmes, Ann; Padia, Janak K.; Roark, William H.; Roth, Bruce D.; Trivedi, Bharat K.; Kleinschroth, Jurgen; Rees, David C.; Richardson, Reginald S.

PA Warner-Lambert Company, USA

SO U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 839, 647, abandoned.

CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 5593967 | A | 19970114 | US 1993-41647 | 19930401 <-- |
| | ZA 9106922 | A | 19930301 | ZA 1991-6922 | 19910830 <-- |
| | US 5846942 | A | 19981208 | US 1996-709316 | 19960909 |
| PRAI | US 1990-576628 | B2 | 19900831 | | |
| | US 1991-726655 | B2 | 19910712 | | |
| | US 1992-839647 | B2 | 19920221 | | |
| | US 1993-41647 | A3 | 19930401 | | |

OS MARPAT 126:199453

AB R1AE(CH2)mCR2(CR5R6R7)n(CH2)pXq(CHR3)r(CHR4)sYt(CR20R12)u(CHR13)vR8 [I; A = bond, O, (alkyl)imino, etc.; E = bond, divalent amino acid residue, (CHR3)r, NHCO, CO2, etc.; R1 = (poly)cycloalkyl, heterocyclyl, etc.; R2,R20 = H, alkyl, vinyl, alkoxy(alkyl), aryl(alkyl), etc.; R3,R4 = groups cited for R2 or (CH2)nBD; B = bond, CO2(CH2)n, CONH(CH2)n, etc.; D = H, OH, CO2H, alkoxy carbonyl, CH2OH, alkoxy methyl, etc.; R5,R6 = H or alkyl; R7,R8 = cycloalkyl, (hetero)aryl, etc.; R12,R13 = H or (CH2)nBD; R12R13 = bond; X,Y = CONH, NHCO, CO2, CH2O, etc.; m,n,p-v = 0-6] were prepared Thus, R1O2CNHCHRCH2R7 (R1 = 2-adamantyl, R7 = 3-indolyl)(II; R = CO2H) was converted in 2 steps to (R)-II (III; R = CHO) which was reductively aminated by (S)-PhCH2CH(NH2)CH2OH to give III [R = (S)-CH2NHCH(CH2OH)CH2Ph]. Data for biol. activity of I were given.

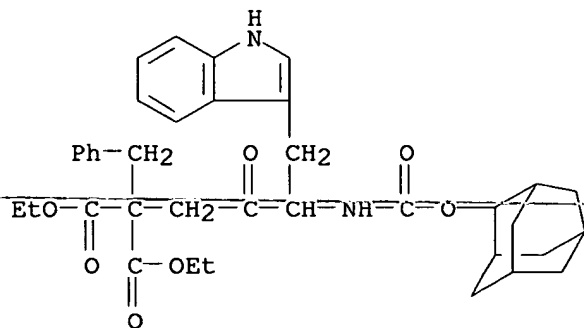
IT 187610-06-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of adamantyl indolylalkylcarbamates and analogs as cholecystokinin antagonists)

RN 187610-06-6 CAPLUS

CN Propanedioic acid, [4-(1H-indol-3-yl)-2-oxo-3-[[tricyclo[3.3.1.1^{3,7}]dec-2-yloxy]carbonyl]amino]butyl] (phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:807715 CAPLUS

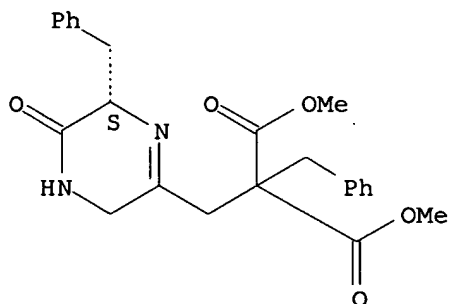
DN 124:29697

TI 3,6-Dioxoperhydropyrrolo[1,2-a]pyrazines as templates for peptidomimetics

AU Martin-Martinez, Mercedes; Garcia-Lopez, M. Teresa; Herranz, Rosario; Gonzalez-Muniz, Rosario

CS Inst. Quim. Med. (CSIC), Madrid, 28006, Spain
 SO Tetrahedron (1995), 51(37), 10361-74
 CODEN: TETRAB; ISSN: 0040-4020
 PB Elsevier
 DT Journal
 LA English
 OS CASREACT 124:29697
 AB The synthesis of 4,7-di- and 4,7,7-trisubstituted 3,6-dioxoperhydropyrrolo[1,2-a]pyrazine-7-carboxylate derivs. was described. The approach used for the preparation of this heterocyclic template was based on the reductive amination of 4-keto diesters derived from dipeptides. E.g., hydrogenation of Me 5-[(N-benzyloxycarbonyl)-L-alanyl]amino-2-methoxycarbonyl-4-oxopentanoate in MeOH in the presence of Pd/C gave 79% (4S,7R,8aR)-7-methoxycarbonyl-4-methyl-3,6-dioxoperhydropyrrolo[1,2-a]pyrazine and 15% (4S,7S,8aS)-7-methoxycarbonyl-4-methyl-3,6-dioxoperhydropyrrolo[1,2-a]pyrazine.
 IT **171513-60-3P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of dioxoperhydropyrrolopyrazines as templates for peptidomimetics)
 RN 171513-60-3 CAPLUS
 CN Propanedioic acid, (phenylmethyl)[[3,4,5,6-tetrahydro-5-oxo-6-(phenylmethyl)pyrazinyl]methyl]-, dimethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 7 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1995:410368 CAPLUS
 DN 122:187373

TI Preparation of polycyclic compounds as phosphodiesterases inhibitors
 IN Tanaka, Masahide; Wakamatsu, Takeshi; Mitsunashi, Hiroshi; Sato, Toshitsugu
 PA Tsumura and Co., Japan
 SO Eur. Pat. Appl., 34 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| PI | EP 594890 | A1 | 19940504 | EP 1992-118620 | 19921030 <-- |
| | R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |

PRAI EP 1992-118620
OS MARPAT 122:187373
GI

19921030

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

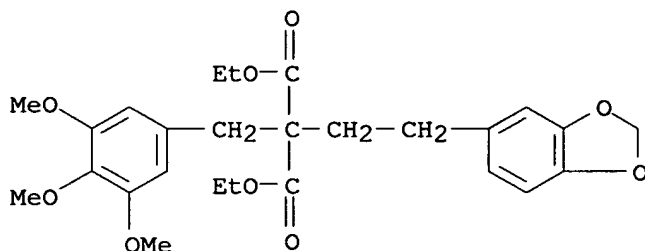
AB Title compds. I (R1-R8 = H, HO, (substituted) alkoxy or PhCH2O, neighboring 2 of R1-R8 = (substituted) alkylene; A = Q wherein X = HC, N), are prepared To (RS)-(E)-3-[1-(3,4-dihydroxy-5-methoxyphenyl)methyl]-(3,4,5-trimethoxybenzylidene)butanol in CH2Cl2 and F3CCO2H was added Fe(ClO4)3 to give (3aRS,SRbiar)-II which at 500 μ M inhibited bovine heart phosphodiesterase 90.5%.

IT 58745-52-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polycyclic compds. as phosphodiesterases inhibitors)

RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 8 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:294083 CAPLUS

DN 123:285785

TI Preparation of aromatic amidine derivatives as inhibitors of human blood coagulation factor for treatment and prevention of influenza

IN Ikeuchi, Kyoshi; Takase, Hiroyuki; Murakami, Yoichi

PA Daiichi Seiyaku Co, Japan

SO Jpn. Kokai Tokkyo Koho, 79 pp.

CODEN: JKXXAF

BT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---------------|------|----------|-----------------|--------------|
| PI | JP 06227971 | A2 | 19940816 | JP 1993-17536 | 19930204 <-- |
| | JP 3457694 | B2 | 20031020 | | |
| PRAI | JP 1993-17536 | | 19930204 | | |

OS MARPAT 123:285785

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R1 = H, alkoxy; R2 = H, alkyl, alkoxy, CO2H, alkoxyacarbonyl, carboxyalkyl, alkoxyacarbonylalkyl; R3 = H, CO2H, alkoxyacarbonyl, carboxyalkyl, alkoxyacarbonylalkyl, carboxyalkoxy, alkoxyacarbonylalkoxy; R4 = H, OH, alkyl, alkoxy; A = C1-4 alkylene which

may be substituted by 1-2 of hydroxyalkyl, CO₂H, alkoxycarbonyl, carboxyalkyl, and alkoxycarbonylalkyl; X = single bond, O, S, CO; Y = 5- or 6-membered (un)saturated carbocyclyl or heterocyclyl, NH₂, or aminoalkyl each of which may be substituted; ring Z = pyrrole, 1,2-dihydropyrrole, furan, thiofuran, imidazole, oxazole, thiazole, benzene, tetrahydrobenzene, or cyclopentadiene ring] are prepared. Thus, Et 3-(5-cyano-2-benzofuranyl)-2-(4-hydroxyphenyl)propionate was condensed with (2S)-1-tert-butoxycarbonyl-2-pyrrolidinemethanol in the presence of Ph₃P and di-Et azodicarboxylate in THF to give ether (II; R = cyano, R₅ = Me₃CO₂C) which was treated with HCl(g) in ethanol and then with NH₃ in EtOH to give amidine II.2HCl (R = amidino, R₅ = H). Title compound (III.2HCl) showed IC₅₀ of 5.04 µg/mL against human blood coagulation.

IT 150610-90-5P 150611-01-1P 150611-03-3P

150613-30-2P 150613-81-3P 167979-40-0P

167979-41-1P 167979-51-3P

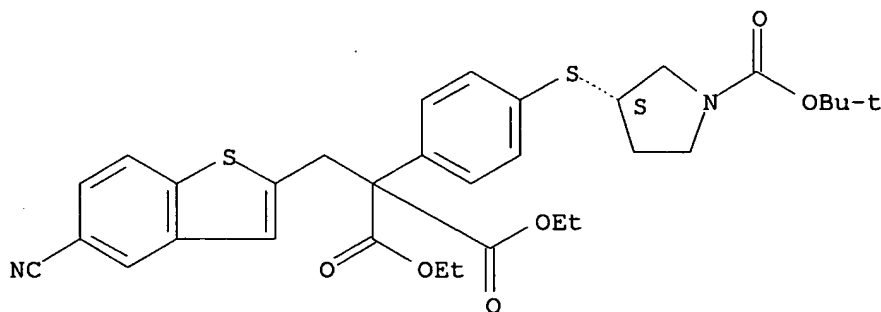
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for preparation of aromatic amidine derivs. as inhibitors of human blood coagulation factor)

RN 150610-90-5 CAPLUS

CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]thio]phenyl]-, diethyl ester, (S)-(9CI) (CA INDEX NAME)

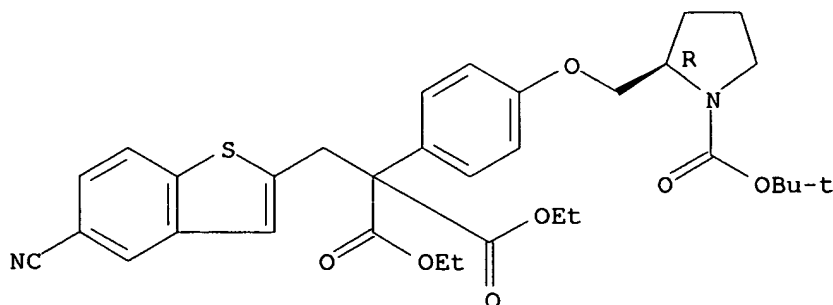
Absolute stereochemistry.



RN 150611-01-1 CAPLUS

CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, (R)-(9CI) (CA INDEX NAME)

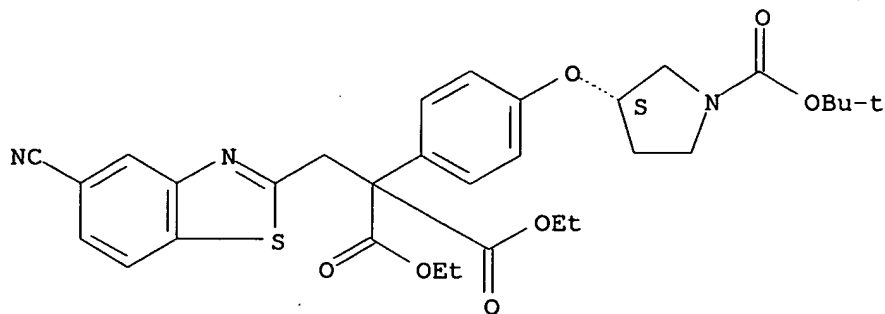
Absolute stereochemistry.



RN 150611-03-3 CAPLUS

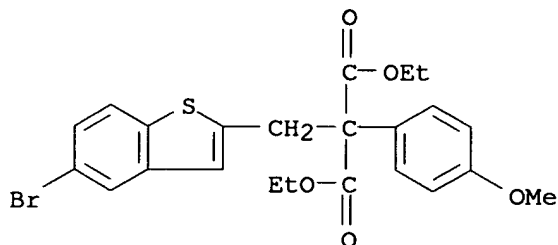
CN Propanedioic acid, [(5-cyano-2-benzothiazolyl)methyl][4-[[[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 150613-30-2 CAPLUS

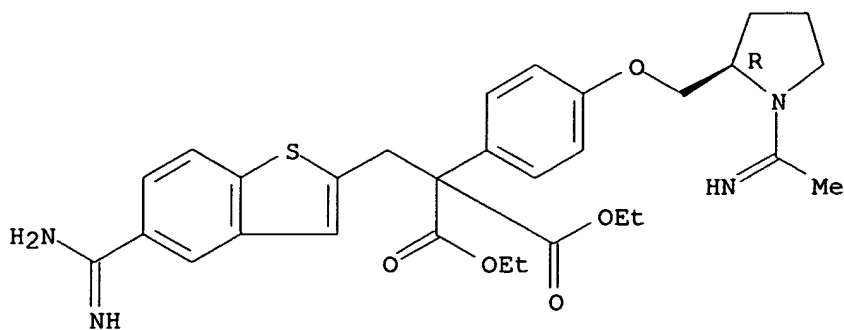
CN Propanedioic acid, [(5-bromobenzo[b]thien-2-yl)methyl](4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 150613-81-3 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][4-[[1-(1-iminoethyl)-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

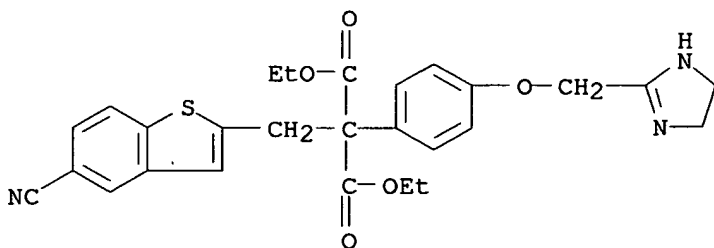
Absolute stereochemistry.



● 2 HCl

RN 167979-40-0 CAPLUS

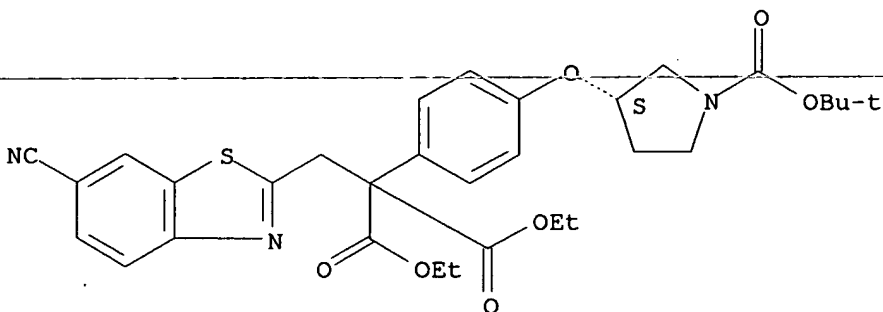
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[(4,5-dihydro-1H-imidazol-2-yl)methoxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 167979-41-1 CAPLUS

CN Propanedioic acid, [(6-cyano-2-benzothiazolyl)methyl][4-[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI) (CA INDEX NAME)

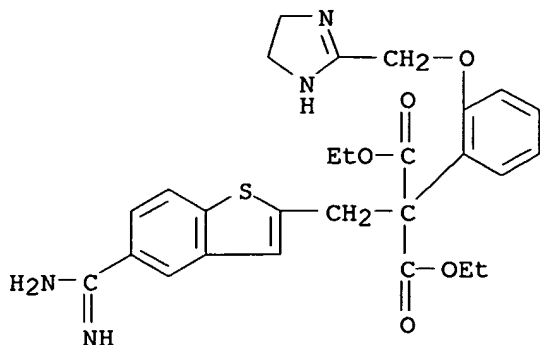
Absolute stereochemistry.



RN 167979-51-3 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][2-[(4,5-dihydro-1H-imidazol-2-yl)methoxy]phenyl]-, diethyl ester,

dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

IT 150613-80-2P

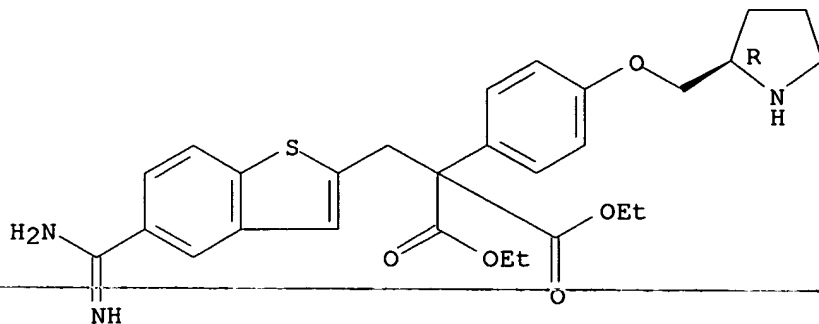
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aromatic amidine derivs. as inhibitors of human blood coagulation factor for treatment and prevention of influenza)

RN 150613-80-2 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L5 ANSWER 9 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1994:107001 CAPLUS

DN 120:107001

TI Heterocyclic and aromatic amidine derivatives and salts thereof

IN Nagahara, Takayasu; Kanaya, Naoaki; Inamura, Kazue; Yokoyama, Yukio

PA Daiichi Pharmaceutical Co., Ltd., Japan

SO Eur. Pat. Appl., 94 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | EP 540051 | A1 | 19930505 | EP 1992-118705 | 19921030 <-- |
| | EP 540051 | B1 | 19960403 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | ZA 9208276 | A | 19930506 | ZA 1992-8276 | 19921026 <-- |
| | IL 103564 | A1 | 19981206 | IL 1992-103564 | 19921027 |
| | NO 9204164 | A | 19930503 | NO 1992-4164 | 19921029 <-- |
| | DE 4236574 | A1 | 19930506 | DE 1992-4236574 | 19921029 <-- |
| | CA 2081836 | AA | 19930501 | CA 1992-2081836 | 19921030 <-- |
| | AU 9227470 | A1 | 19930506 | AU 1992-27470 | 19921030 <-- |
| | AU 666137 | B2 | 19960201 | | |
| | JP 05208946 | A2 | 19930820 | JP 1992-292892 | 19921030 <-- |
| | JP 2879718 | B2 | 19990405 | | |
| | US 5300851 | A | 19940405 | US 1992-969369 | 19921030 <-- |
| | HU 65890 | A2 | 19940728 | HU 1992-3433 | 19921030 <-- |
| | AT 136293 | E | 19960415 | AT 1992-118705 | 19921030 <-- |
| | ES 2088073 | T3 | 19960801 | ES 1992-118705 | 19921030 <-- |
| | PL 170312 | B1 | 19961129 | PL 1992-296439 | 19921030 <-- |
| | JP 10291931 | A2 | 19981104 | JP 1998-85454 | 19921030 <-- |
| | JP 3461441 | B2 | 20031027 | | |
| | CZ 284381 | B6 | 19981111 | CZ 1992-3276 | 19921030 <-- |
| | SK 279807 | B6 | 19990413 | SK 1992-3276 | 19921030 |
| | RU 2139851 | C1 | 19991020 | RU 1992-4542 | 19921030 |
| | SG 78251 | A1 | 20010220 | SG 1996-6031 | 19921030 |
| | FI 107923 | B1 | 20011031 | FI 1992-4932 | 19921030 |
| | CN 1072677 | A | 19930602 | CN 1992-114304 | 19921031 <-- |
| | CN 1049434 | B | 20000216 | | |
| | KR 205152 | B1 | 19990701 | KR 1992-20309 | 19921031 |
| | BG 63237 | B2 | 20010629 | BG 1994-98594 | 19940225 |
| | US 5576343 | A | 19961119 | US 1995-468304 | 19950606 <-- |
| | US 5620991 | A | 19970415 | US 1995-471173 | 19950606 <-- |
| | CN 1168885 | A | 19971231 | CN 1997-110745 | 19970416 <-- |
| | CN 1097052 | B | 20021225 | | |
| | CN 1168886 | A | 19971231 | CN 1997-110748 | 19970416 <-- |
| | CN 1062865 | B | 20010307 | | |
| | US 5866577 | A | 19990202 | US 1997-924504 | 19970905 |
| | US 5962695 | A | 19991005 | US 1998-131235 | 19980807 |
| PRAI | JP 1991-286088 | A | 19911031 | | |
| | JP 1991-285919 | A | 19911031 | | |
| | JP 1992-292892 | A3 | 19921030 | | |
| | US 1992-969369 | B1 | 19921030 | | |
| | US 1992-969396 | B1 | 19921030 | | |
| | US 1994-282571 | B3 | 19940729 | | |
| | US 1995-469593 | A1 | 19950606 | | |
| | US 1997-924504 | A3 | 19970905 | | |
| OS | MARPAT 120:107001 | | | | |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | The title compds. I (where the benzeno-2 ring is indolyl, benzimidazolyl, naphthyl, etc.; R = HN:CNH2; R1 = H, alkoxy; R2 = H, alkyl, alkoxy, etc.; R3 = H, carboxyl, etc.; R4 = H, OH, alkyl, alkoxy; A = C1-4 alkylene; X = single bond, O, S, CO; n = 0-4; Y = heterocyclic or cyclic hydrocarbon | | | | |

moiety) useful as anticoagulant agents were prepared by treating I (R = CN) with R₅OH (R₅ = alkyl) to give I (R = R₅OC:NH) followed by treatment with NH₃. Some of the prepared compds. showed strong anticoagulant activity through their specific anti-FXa activity in comparison with DABE.

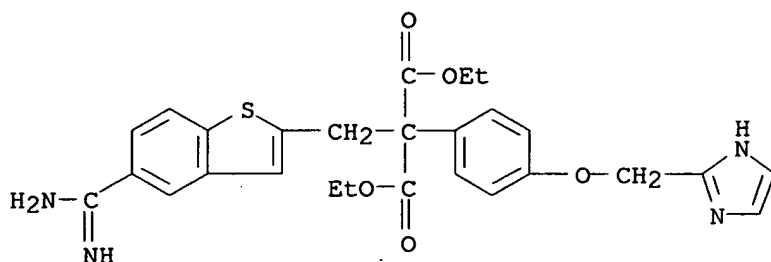
IT 150613-79-9P 150613-81-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrolysis of)

RN 150613-79-9 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][4-(1H-imidazol-2-ylmethoxy)phenyl]-, diethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

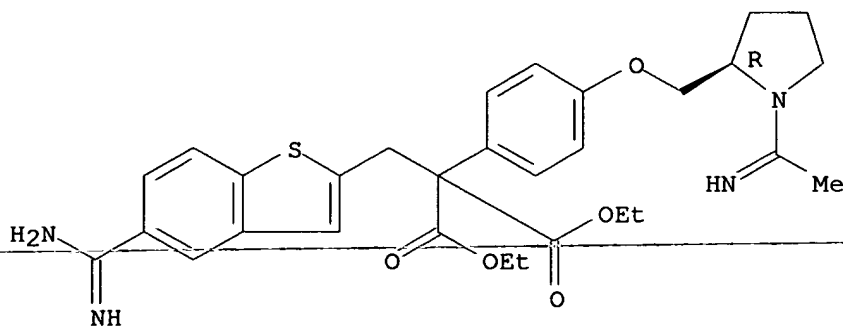


●2 HCl

RN 150613-81-3 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][4-[[1-(1-iminoethyl)-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

IT 150610-90-5P 150611-01-1P 150611-02-2P

150611-03-3P 150613-30-2P

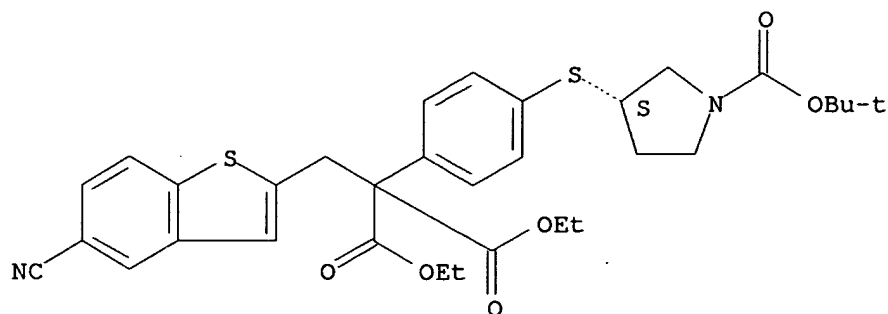
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of amidine anticoagulants)

RN 150610-90-5 CAPLUS

CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]thio]phenyl]-, diethyl ester, (S)-(9CI) (CA INDEX NAME)

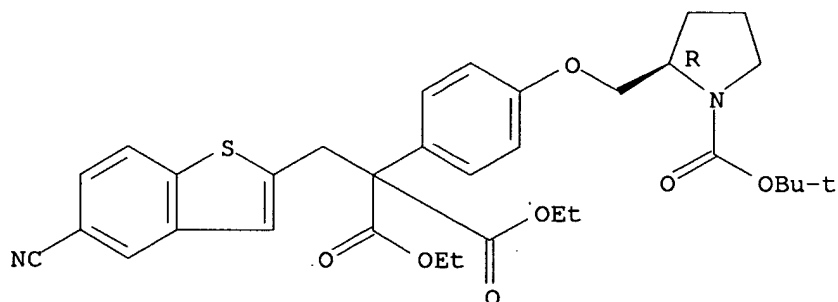
Absolute stereochemistry.



RN 150611-01-1 CAPLUS

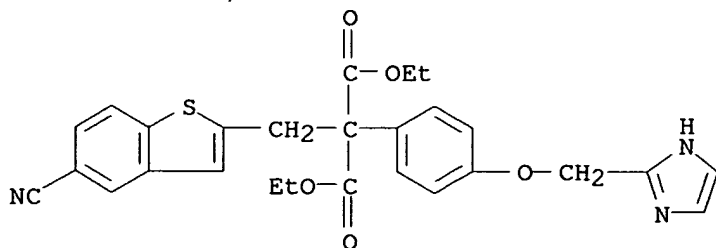
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-[[1-[(1,1-dimethylethoxy)carbonyl]-2-pyrrolidinyl]methoxy]phenyl]-, diethyl ester, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150611-02-2 CAPLUS

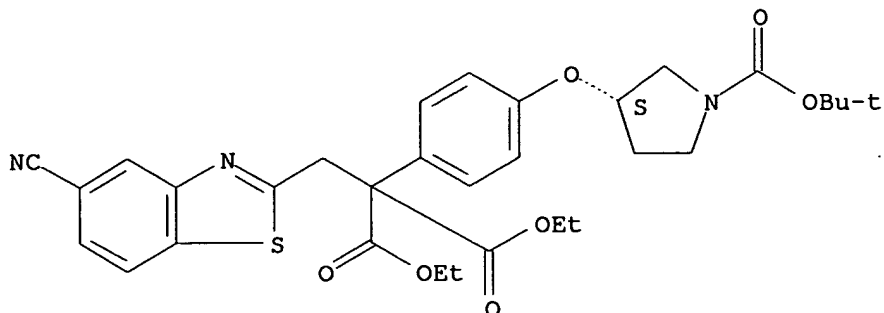
CN Propanedioic acid, [(5-cyanobenzo[b]thien-2-yl)methyl][4-(1H-imidazol-2-ylmethoxy)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 150611-03-3 CAPLUS

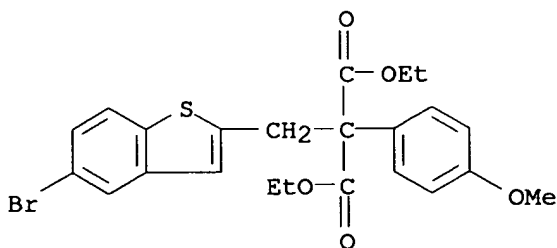
CN Propanedioic acid, [(5-cyano-2-benzothiazolyl)methyl][4-[[[(3S)-1-[(1,1-dimethylethoxy)carbonyl]-3-pyrrolidinyl]oxy]phenyl]-, diethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 150613-30-2 CAPLUS

CN Propanedioic acid, [(5-bromobenzo[b]thien-2-yl)methyl](4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



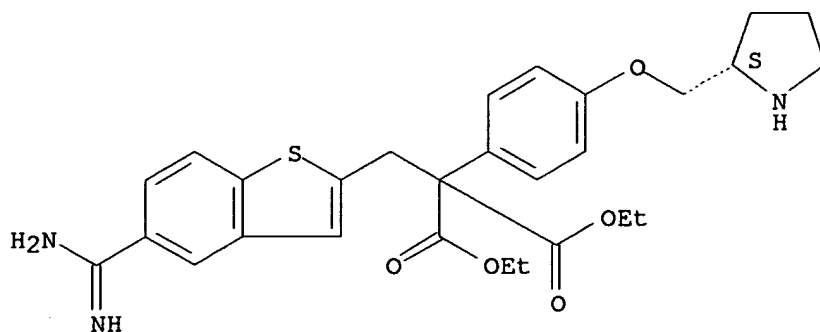
IT 150612-15-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anticoagulants)

RN 150612-15-0 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl)methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

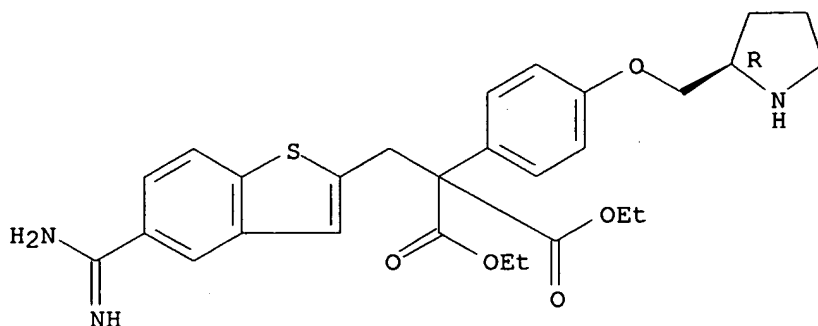
IT 150613-80-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Et acetimidate)

RN 150613-80-2 CAPLUS

CN Propanedioic acid, [[5-(aminoiminomethyl)benzo[b]thien-2-yl]methyl][4-(2-pyrrolidinylmethoxy)phenyl]-, diethyl ester, dihydrochloride, (R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L5 ANSWER 10 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:603418 CAPLUS

DN 119:203418

TI Preparation ofazole derivative herbicides and fungicides

IN West, Peter John; Cornell, Clive Leonard; Briggs, Geoffrey Gower;
Buehmann, Ulrich

PA Schering Agrochemicals Ltd., UK

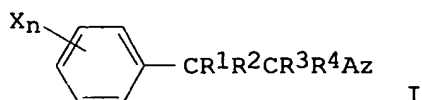
SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9311118 | A1 | 19930610 | WO 1992-EP2723 | 19921125 <-- |
| | W: AU, BG, BR, CA, CS, FI, HU, JP, KR, NO, PL, RO, RU, SD, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| | AU 9229458 | A1 | 19930628 | AU 1992-29458 | 19921125 <-- |
| | EP 619812 | A1 | 19941019 | EP 1992-923799 | 19921125 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | JP 07501801 | T2 | 19950223 | JP 1992-509801 | 19921125 <-- |
| | HU 68182 | A2 | 19950313 | HU 1994-1466 | 19921125 <-- |
| | BR 9206862 | A | 19951121 | BR 1992-6862 | 19921125 <-- |
| | ZA 9209336 | A | 19930802 | ZA 1992-9336 | 19921202 <-- |
| | CN 1075478 | A | 19930825 | CN 1992-115306 | 19921204 <-- |
| | FI 9402596 | A | 19940602 | FI 1994-2596 | 19940602 <-- |
| PRAI | GB 1991-25791 | A | 19911204 | | |
| | WO 1992-EP2723 | A | 19921125 | | |
| OS | MARPAT 119:203418 | | | | |
| GI | | | | | |



AB Title compds. I (Az = imidazol-1-yl, 1,2,4-triazol-1-yl; X = halo, HO₂C, O₂N, NC, R₅O₂C wherein R₅ = (substituted) alkenyl, etc.; R₁ = R₅CO, R₅O₂C, HS, R₅(O)_pS wherein p = 0-2; R₂ = NC, R₅CO, O₂N, aryl, aralkyl, heteroaryl, etc.; R₃, R₄ = H, (substituted) alkyl, aryl, heteroaryl; n = 0-4), are prepared 2,4-Cl₂C₆H₃CH₂CO₂Pr (preparation given) was added to lithium

diisopropylamide in THF followed by ClCO₂Pr to give di-Pr (2,4-dichlorophenyl)malonate which in MeOCH₂CH₂OMe was treated with NaI and 1-(chloromethyl)-1H-1,2,4-triazole to give I (Az = 1,2,4-triazol-1-yl, X_n = 2,4-Cl₂C₆H₃, R₁ = R₂ = Pro₂C, R₃ = R₄ = H). A similar prepared compound I (Az = 1,2,4-triazol-1-yl, X_n = 2-(OMe)C₆H₄, R₁ = R₂ = Pro₂C, R₃ = R₄ = H) at 2.0 kg/ha was effective 90-100% against blackgrass, couch, scentless mayweed and Buxbaum's speedwell.

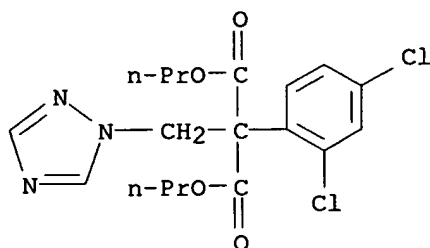
IT 150441-89-7P 150441-91-1P 150441-92-2P
150441-93-3P 150441-94-4P 150441-95-5P
~~150441-96-6P 150441-97-7P 150441-98-8P~~
150441-99-9P 150442-00-5P 150442-01-6P
150442-02-7P 150442-03-8P 150442-04-9P
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 150442-86-7P 150442-87-8P 150442-88-9P
 150442-89-0P 150442-91-4P 150443-02-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as agrochem. fungicide and herbicide)

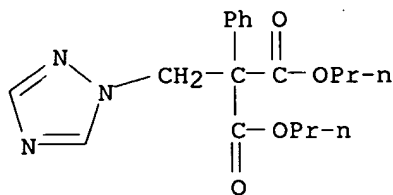
RN 150441-89-7 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



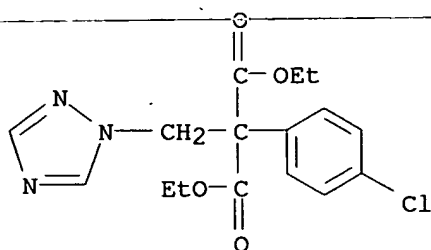
RN 150441-91-1 CAPLUS

CN Propanedioic acid, phenyl (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



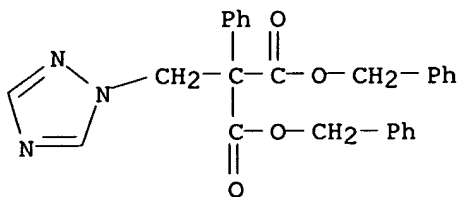
RN 150441-92-2 CAPLUS

CN Propanedioic acid, (4-chlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



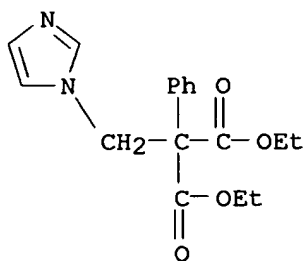
RN 150441-93-3 CAPLUS

CN Propanedioic acid, phenyl (1H-1,2,4-triazol-1-ylmethyl)-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



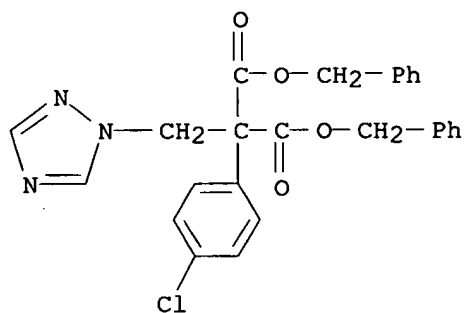
RN 150441-94-4 CAPLUS

CN Propanedioic acid, (1H-imidazol-1-ylmethyl)phenyl-, diethyl ester (9CI)
(CA INDEX NAME)



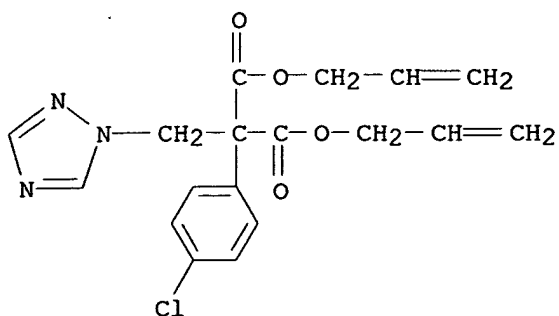
RN 150441-95-5 CAPLUS

CN Propanedioic acid, (4-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-,
bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

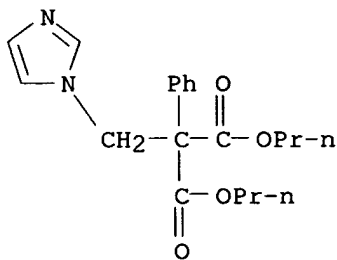


RN 150441-96-6 CAPLUS

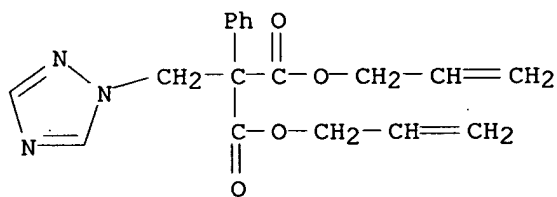
CN Propanedioic acid, (4-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-,
di-2-propenyl ester (9CI) (CA INDEX NAME)



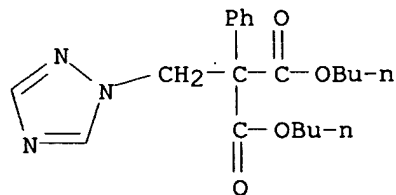
RN 150441-97-7 CAPLUS

CN Propanedioic acid, (1H-imidazol-1-ylmethyl)phenyl-, dipropyl ester (9CI)
(CA INDEX NAME)

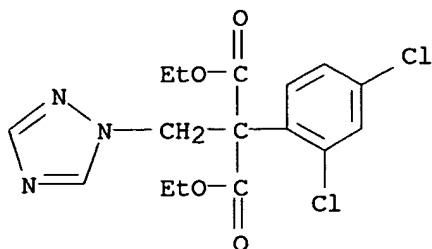
RN 150441-98-8 CAPLUS

CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, di-2-propenyl
ester (9CI) (CA INDEX NAME)

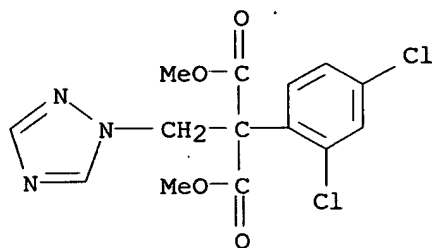
RN 150441-99-9 CAPLUS

CN Propanedioic acid, phenyl(1H-1,2,4-triazol-1-ylmethyl)-, dibutyl ester
(9CI) (CA INDEX NAME)

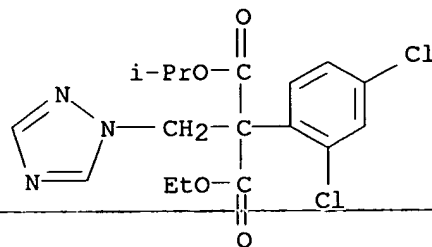
RN 150442-00-5 CAPLUS
 CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



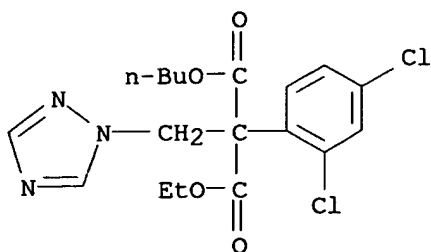
RN 150442-01-6 CAPLUS
 CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



RN 150442-02-7 CAPLUS
 CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, ethyl 1-methylethyl ester (9CI) (CA INDEX NAME)

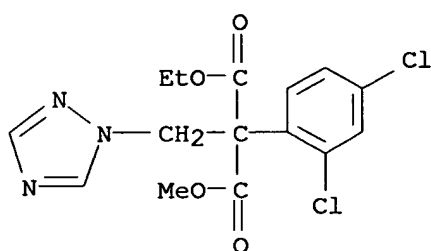


RN 150442-03-8 CAPLUS
 CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, butyl ethyl ester (9CI) (CA INDEX NAME)



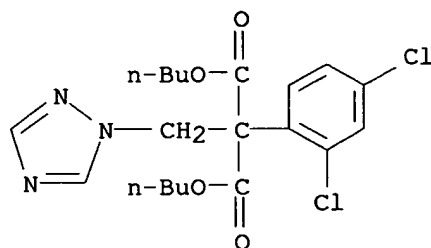
RN 150442-04-9 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, ethyl methyl ester (9CI) (CA INDEX NAME)



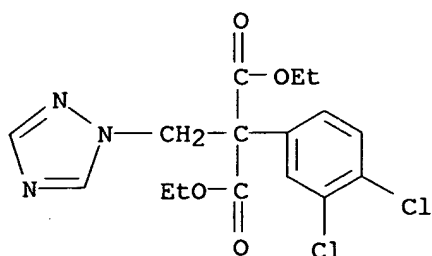
RN 150442-07-2 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dibutyl ester (9CI) (CA INDEX NAME)



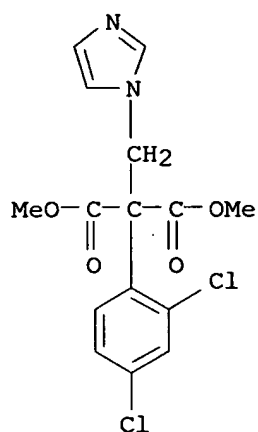
RN 150442-08-3 CAPLUS

CN Propanedioic acid, (3,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



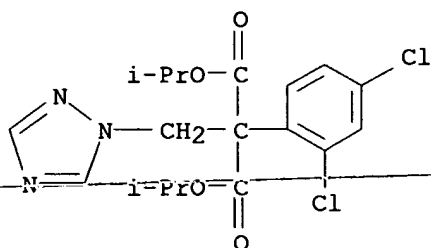
RN 150442-09-4 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



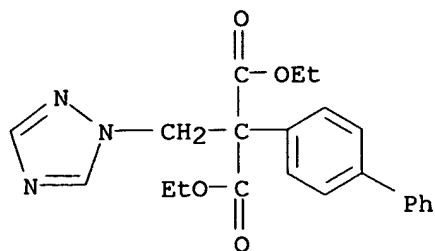
RN 150442-10-7 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



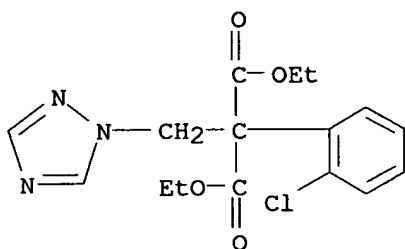
RN 150442-11-8 CAPLUS

CN Propanedioic acid, [1,1'-biphenyl]-4-yl(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



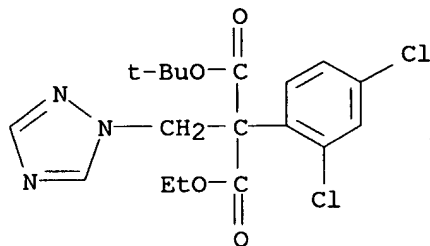
RN 150442-12-9 CAPLUS

CN Propanedioic acid, (2-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



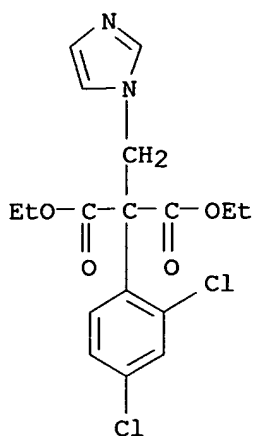
RN 150442-13-0 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, 1,1-dimethylethyl ethyl ester (9CI) (CA INDEX NAME)



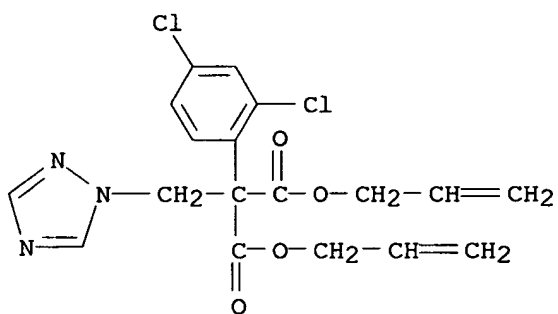
RN 150442-15-2 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



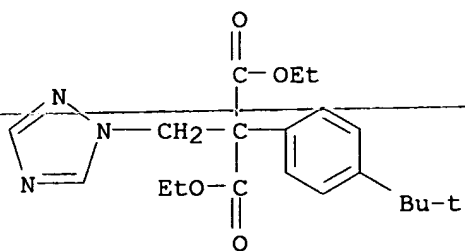
RN 150442-16-3 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, di-2-propenyl ester (9CI) (CA INDEX NAME)



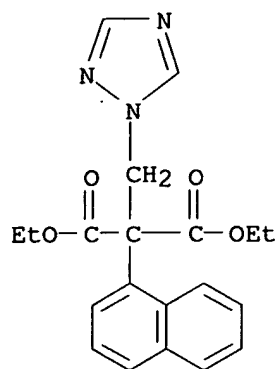
RN 150442-19-6 CAPLUS

CN Propanedioic acid, [4-(1,1-dimethylethyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



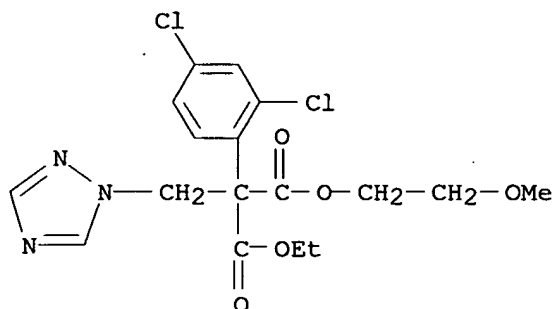
RN 150442-23-2 CAPLUS

CN Propanedioic acid, 1-naphthalenyl(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



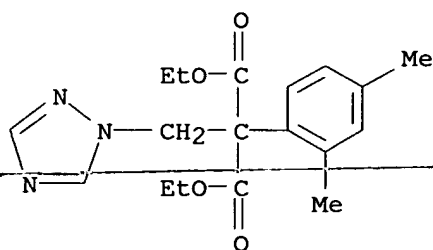
RN 150442-24-3 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, ethyl 2-methoxyethyl ester (9CI) (CA INDEX NAME)



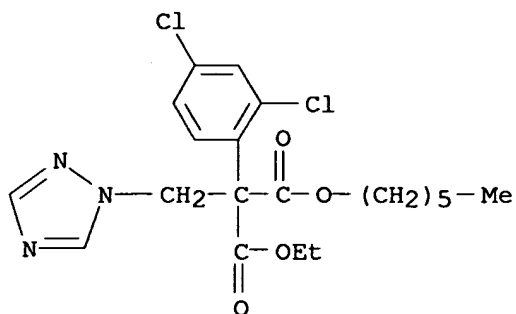
RN 150442-28-7 CAPLUS

CN Propanedioic acid, (2,4-dimethylphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



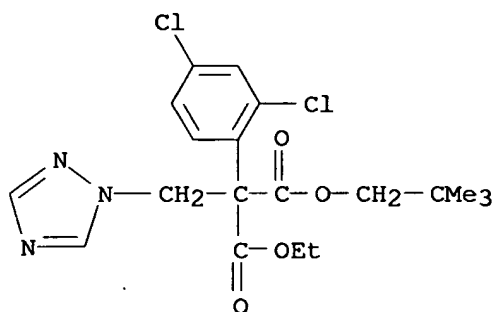
RN 150442-30-1 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, ethyl hexyl ester (9CI) (CA INDEX NAME)



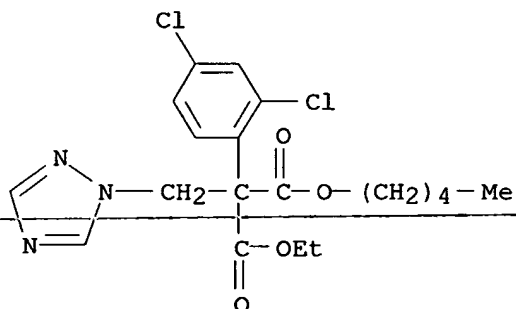
RN 150442-31-2 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, 2,2-dimethylpropyl ethyl ester (9CI) (CA INDEX NAME)



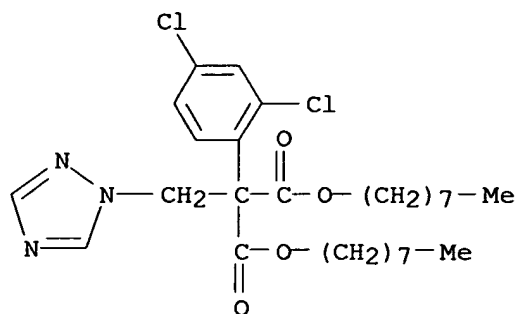
RN 150442-32-3 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, ethyl pentyl ester (9CI) (CA INDEX NAME)



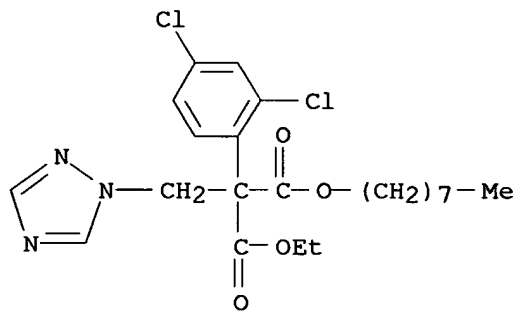
RN 150442-33-4 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dioctyl ester (9CI) (CA INDEX NAME)



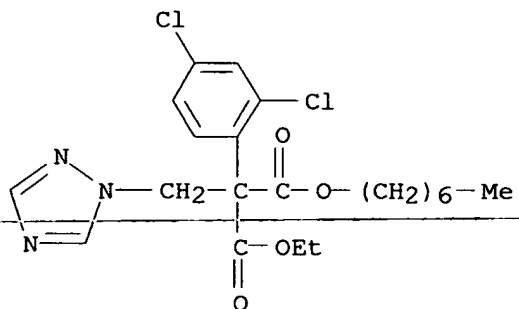
RN 150442-34-5 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl octyl ester (9CI) (CA INDEX NAME)



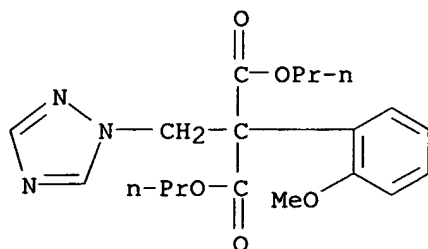
RN 150442-35-6 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, ethyl heptyl ester (9CI) (CA INDEX NAME)



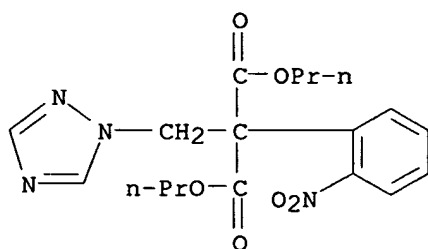
RN 150442-36-7 CAPLUS

CN Propanedioic acid, (2-methoxyphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



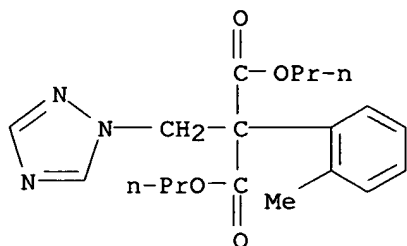
RN 150442-37-8 CAPLUS

CN Propanedioic acid, (2-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



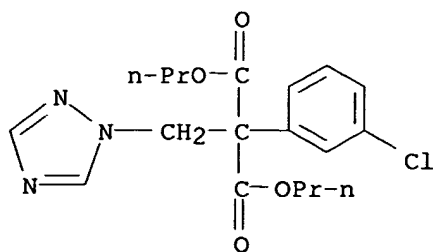
RN 150442-38-9 CAPLUS

CN Propanedioic acid, (2-methylphenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



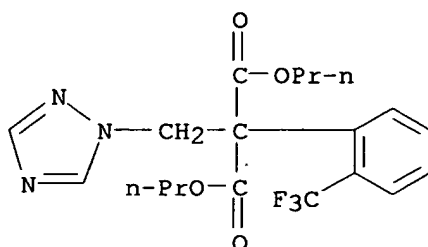
RN 150442-39-0 CAPLUS

CN Propanedioic acid, (3-chlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



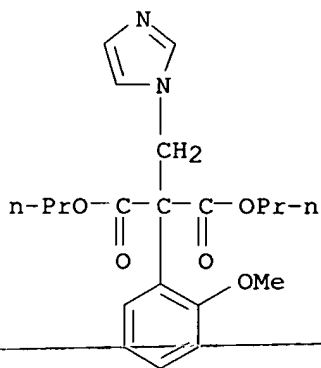
RN 150442-40-3 CAPLUS

CN Propanedioic acid, (1H-1,2,4-triazol-1-ylmethyl) [2-(trifluoromethyl)phenyl]-, dipropyl ester (9CI) (CA INDEX NAME)



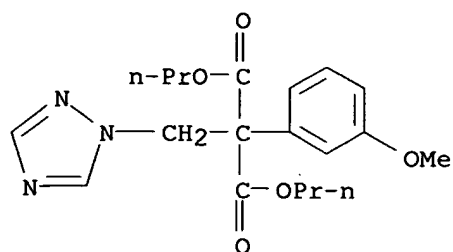
RN 150442-41-4 CAPLUS

CN Propanedioic acid, (1H-imidazol-1-ylmethyl) (2-methoxyphenyl)-, dipropyl ester (9CI) (CA INDEX NAME)



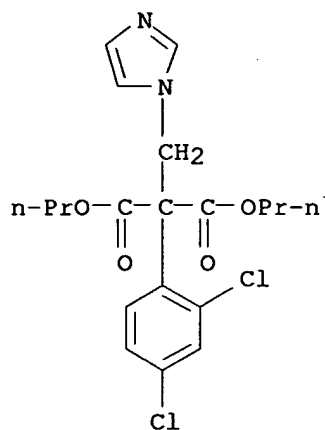
RN 150442-43-6 CAPLUS

CN Propanedioic acid, (3-methoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



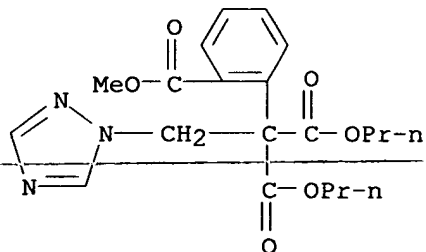
RN 150442-44-7 CAPLUS

CN Propanedioic acid, (2,4-dichlorophenyl)(1H-imidazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



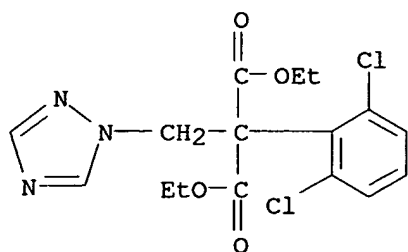
RN 150442-45-8 CAPLUS

CN Propanedioic acid, [2-(methoxycarbonyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



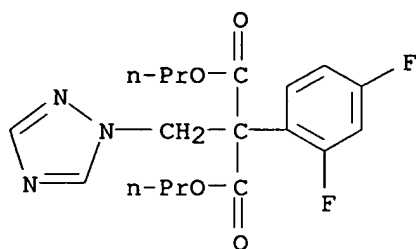
RN 150442-47-0 CAPLUS

CN Propanedioic acid, (2,6-dichlorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



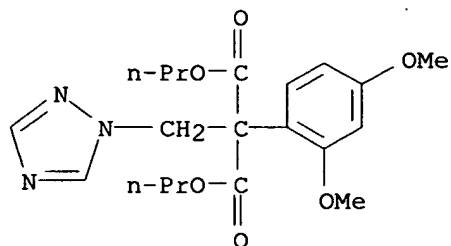
RN 150442-51-6 CAPLUS

CN Propanedioic acid, (2,4-difluorophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



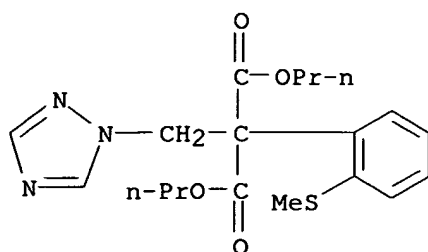
RN 150442-52-7 CAPLUS

CN Propanedioic acid, (2,4-dimethoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



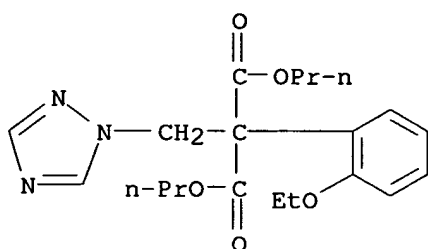
RN 150442-55-0 CAPLUS

CN Propanedioic acid, [2-(methylthio)phenyl] (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



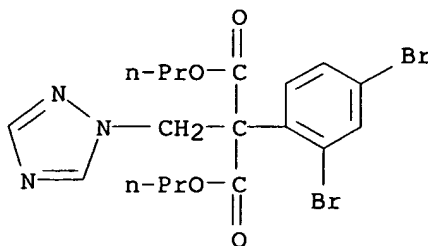
RN 150442-56-1 CAPLUS

CN Propanedioic acid, (2-ethoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



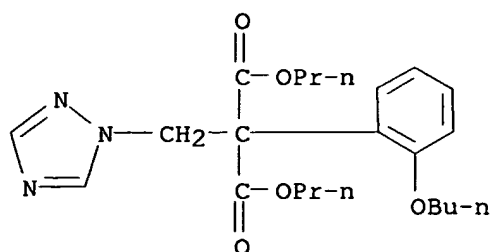
RN 150442-58-3 CAPLUS

CN Propanedioic acid, (2,4-dibromophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



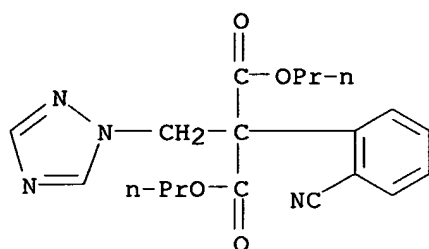
RN 150442-61-8 CAPLUS

CN Propanedioic acid, (2-butoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



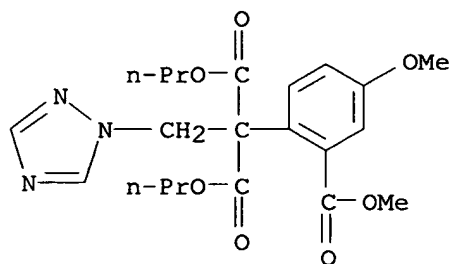
RN 150442-62-9 CAPLUS

CN Propanedioic acid, (2-cyanophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



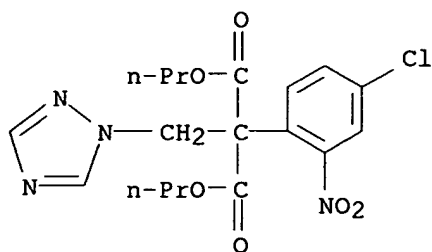
RN 150442-69-6 CAPLUS

CN Propanedioic acid, [4-methoxy-2-(methoxycarbonyl)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



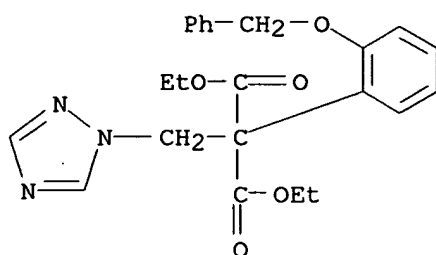
RN 150442-70-9 CAPLUS

CN Propanedioic acid, (4-chloro-2-nitrophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



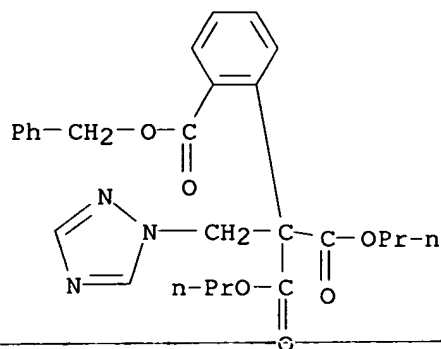
RN 150442-71-0 CAPLUS

CN Propanedioic acid, [2-(phenylmethoxy)phenyl] (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



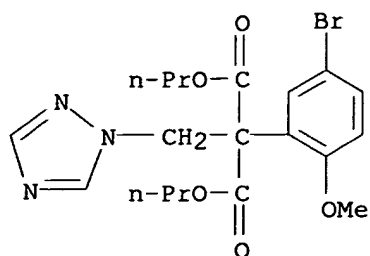
RN 150442-72-1 CAPLUS

CN Propanedioic acid, [2-[(phenylmethoxy)carbonyl]phenyl] (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



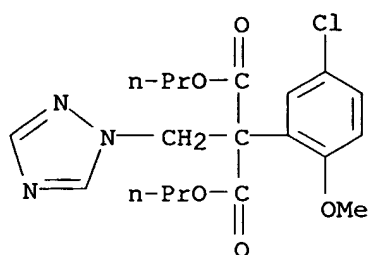
RN 150442-73-2 CAPLUS

CN Propanedioic acid, (5-bromo-2-methoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



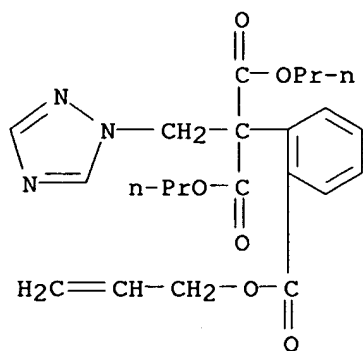
RN 150442-76-5 CAPLUS

CN Propanedioic acid, (5-chloro-2-methoxyphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



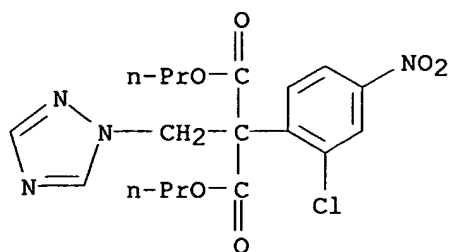
RN 150442-77-6 CAPLUS

CN Propanedioic acid, [2-[(2-propenyloxy)carbonyl]phenyl] (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



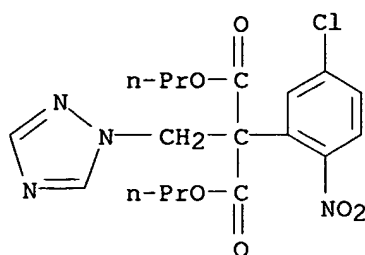
RN 150442-78-7 CAPLUS

CN Propanedioic acid, (2-chloro-4-nitrophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



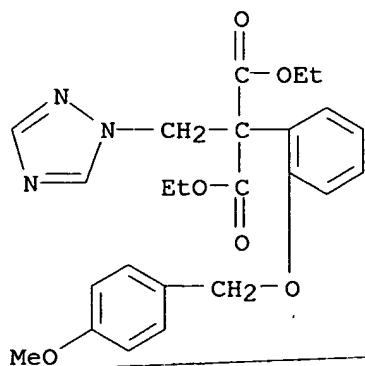
RN 150442-84-5 CAPLUS

CN Propanedioic acid, (5-chloro-2-nitrophenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



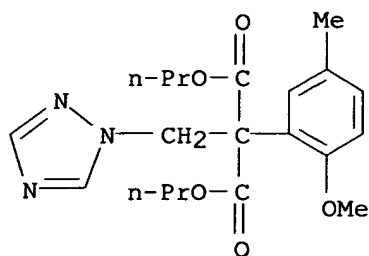
RN 150442-86-7 CAPLUS

CN Propanedioic acid, [2-[(4-methoxyphenyl)methoxy]phenyl] (1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



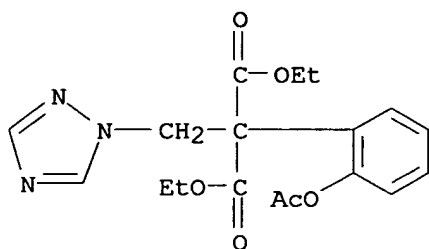
RN 150442-87-8 CAPLUS

CN Propanedioic acid, (2-methoxy-5-methylphenyl) (1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



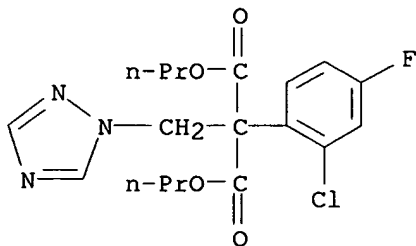
RN 150442-88-9 CAPLUS

CN Propanedioic acid, [2-(acetyloxy)phenyl](1H-1,2,4-triazol-1-ylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



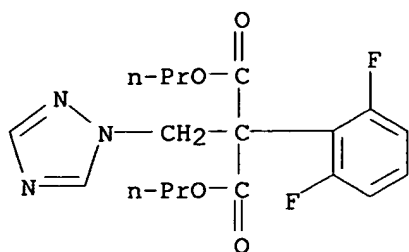
RN 150442-89-0 CAPLUS

CN Propanedioic acid, (2-chloro-4-fluorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)

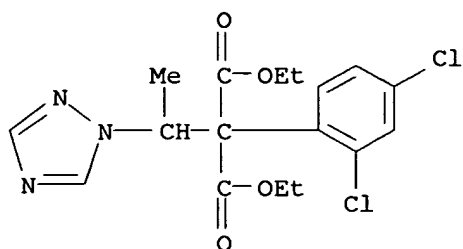


RN 150442-91-4 CAPLUS

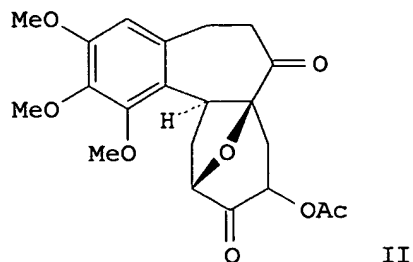
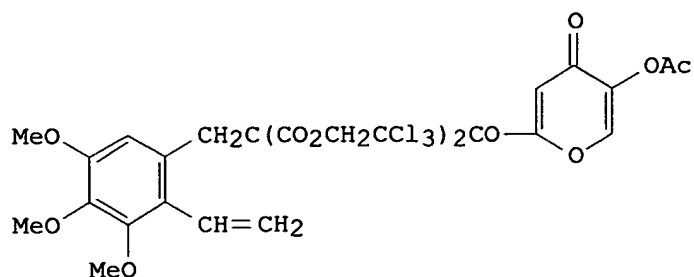
CN Propanedioic acid, (2,6-difluorophenyl)(1H-1,2,4-triazol-1-ylmethyl)-, dipropyl ester (9CI) (CA INDEX NAME)



RN 150443-02-0 CAPLUS
 CN Propanedioic acid, (2,4-dichlorophenyl)[1-(1H-1,2,4-triazol-1-yl)ethyl]-,
 diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 11 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1993:517588 CAPLUS
 DN 119:117588
 TI Cycloadditions of 4-pyrones. An approach to colchicine
 AU McBride, Bill J.; Garst, Michael E.
 CS Dep. Chem., Univ. California, San Diego, La Jolla, CA, 92093, USA
 SO Tetrahedron (1993), 49(14), 2839-54
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA English
 OS CASREACT 119:117588
 GI



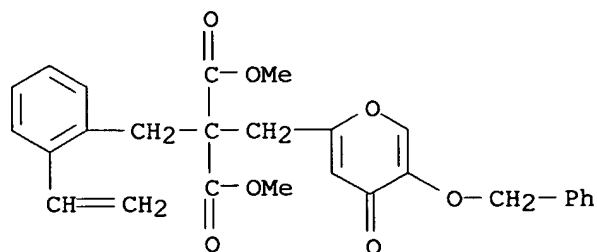
AB The 4-pyrone, [5-acetoxy-4-oxo-4H-pyran-2-yl]carbonyl chloride was coupled with the malonate anion of bis(2,2,2-trichloroethyl) 2-ethenyl-3,4,5-trimethoxybenzylpropanedioate and analogs thereof to give the pyranylcarbonyl(ethenylbenzyl)propanedioate adduct I and the corresponding analogs. These adducts then underwent intramol. thermal cyclizations (61-100% yield) to form the two fused seven member rings of the carbon skeleton of colchicine. The malonate moiety was deprotected and decarboxylated quant. to provide the desired epoxybenzoheptalenedione II which contained a bridging ether, from C7a to C11 in the C ring, and a ketone at the 7 position. Removal of the bridging ether as H₂O would yield the desired tropolone. Attempts to remove the ether bridge were unsuccessful.

IT **149296-22-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

RN 149296-22-0 CAPLUS

CN Propanedioic acid, [(2-ethenylphenyl)methyl][[4-oxo-5-(phenylmethoxy)-4H-pyran-2-yl]methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



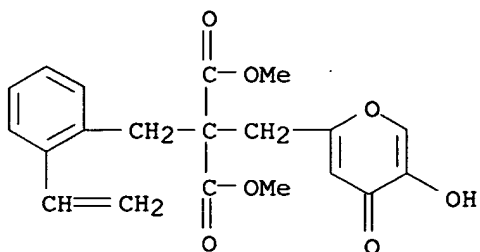
IT **87057-53-2P 149295-99-8P 149296-01-5P
149296-03-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and intramol. cyclization of)

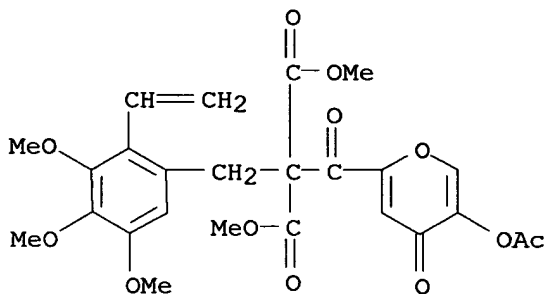
RN 87057-53-2 CAPLUS

CN Propanedioic acid, [(2-ethenylphenyl)methyl][(5-hydroxy-4-oxo-4H-pyran-2-yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



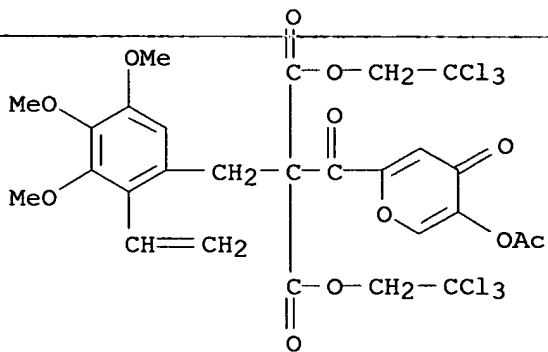
RN 149295-99-8 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



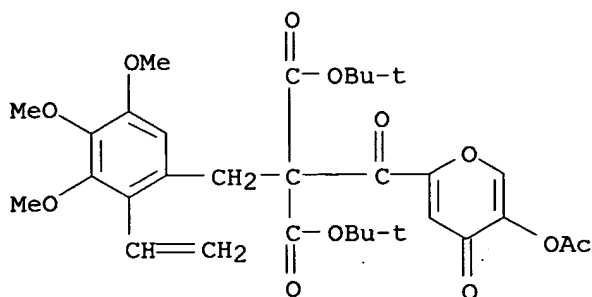
RN 149296-01-5 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 149296-03-7 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-ethenyl-3,4,5-trimethoxyphenyl)methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



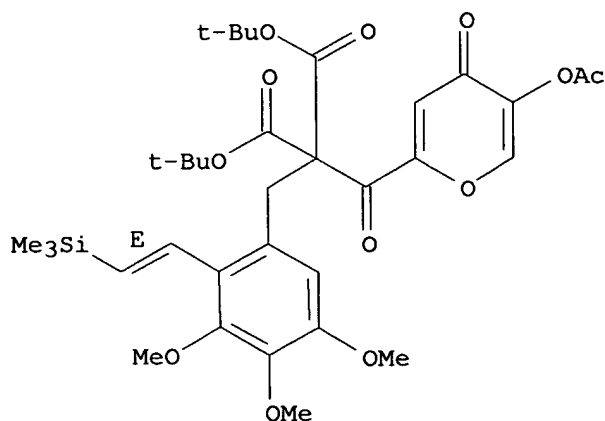
IT 149296-05-9P 149296-06-0P 149296-07-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 149296-05-9 CAPLUS

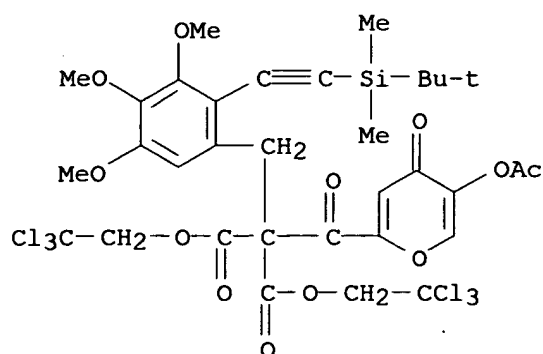
CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(3,4,5-trimethoxy-2-[2-(trimethylsilyl)ethenyl]phenyl)methyl]-, bis(1,1-dimethylethyl) ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



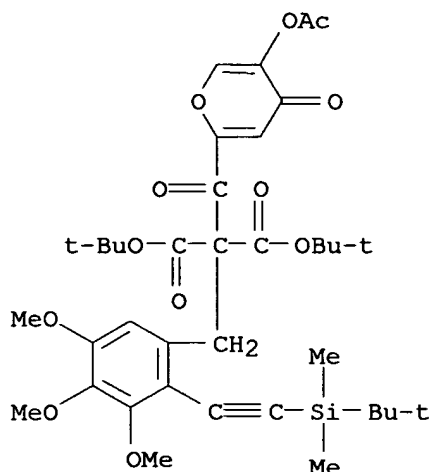
RN 149296-06-0 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][(2-[[[(1,1-dimethylethyl)dimethylsilyl]ethynyl]-3,4,5-trimethoxyphenyl)methyl]-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 149296-07-1 CAPLUS

CN Propanedioic acid, [[5-(acetyloxy)-4-oxo-4H-pyran-2-yl]carbonyl][[2-[[[(1,1-dimethylethyl)dimethylsilyl]ethynyl]-3,4,5-trimethoxyphenyl]methyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L5 ANSWER 12 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:73665 CAPLUS

~~DN 118:73665~~

TI Use of angiotensin II receptor antagonists in the treatment of diabetic nephropathy

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

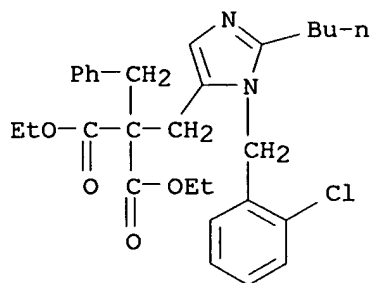
DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | WO 9210182 | A1 | 19920625 | WO 1991-GB2220 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |

AU 9190585 A1 19920708 AU 1991-90585 19911212 <--
 EP 561939 A1 19930929 EP 1992-901222 19911212 <--
 EP 561939 B1 19980218
 R: BE, CH, DE, FR, GB, IT, LI, NL
 JP 06503343 T2 19940414 JP 1992-502130 19911212 <--
 JP 3512793 B2 20040331
 US 6028091 A 20000222 US 1999-371673 19990810
 PRAI GB 1990-27210 A 19901214
 WO 1991-GB2220 W 19911212
 US 1995-375028 B1 19950119
 US 1995-535796 B1 19950928
 US 1996-732027 B1 19961016
 US 1997-901460 B1 19970728
 US 1999-277922 B1 19990329
 OS MARPAT 118:73665
 AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating diabetic nephropathy.
 Preparation of
 3-[2-n-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal saline.
 IT **141771-33-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, in angiotensin II receptor antagonist preparation
 for diabetic nephropathy treatment)
 RN 141771-33-7 CAPLUS
 CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 13 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1992:605225 CAPLUS
 DN 117:205225
 TI Use of angiotensin II receptor antagonists for the preparation of a medicament for improving cognitive function
 IN Hill, James
 PA Smithkline Beecham PLC, UK
 SO PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DT Patent
 LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | WO 9210186 | A1 | 19920625 | WO 1991-GB2224 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190692 | A1 | 19920708 | AU 1991-90692 | 19911212 <-- |
| | EP 561896 | A1 | 19930929 | EP 1992-900687 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503338 | T2 | 19940414 | JP 1992-501731 | 19911212 <-- |
| | US 2002055490 | A1 | 20020509 | US 2001-794723 | 20010227 |
| | US 2003096851 | A1 | 20030522 | US 2002-287955 | 20021105 |
| | US 2003187044 | A1 | 20031002 | US 2003-404345 | 20030401 |

| | | | | | |
|------|----------------|----|----------|--|--|
| PRAI | GB 1990-27197 | A | 19901214 | | |
| | WO 1991-GB2224 | A | 19911212 | | |
| | US 1993-74811 | B1 | 19930610 | | |
| | US 1994-325749 | B1 | 19941019 | | |
| | US 1995-437000 | B1 | 19950508 | | |
| | US 1995-568846 | B1 | 19951207 | | |
| | US 1997-835692 | B1 | 19970410 | | |
| | US 1998-82010 | B1 | 19980520 | | |
| | US 1999-252725 | B1 | 19990219 | | |
| | US 1999-371362 | B1 | 19990810 | | |
| | US 1999-456868 | B1 | 19991208 | | |
| | US 2001-794723 | A1 | 20010227 | | |
| | US 2002-287955 | B1 | 20021105 | | |

OS MARPAT 117:205225

AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for improving cognitive function. Preparation of

3-[2-n-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal saline.

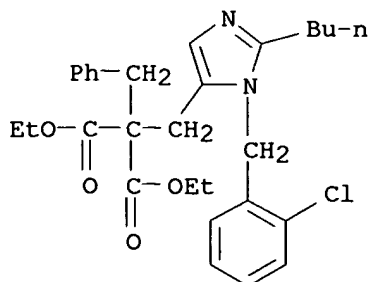
IT 141771-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in angiotensin II receptor antagonist preparation for improving cognitive function)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1992:605208 CAPLUS
 DN 117:205208
 TI Use of angiotensin II receptor antagonists in the treatment of hemorrhagic stroke
 IN Hill, James
 PA Smithkline Beecham PLC, UK
 SO PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9210188 | A1 | 19920625 | WO 1991-GB2226 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190841 | A1 | 19920708 | AU 1991-90841 | 19911212 <-- |
| | EP 561977 | A1 | 19930929 | EP 1992-901997 | 19911212 <-- |
| | EP 561977 | B1 | 20040526 | | |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503558 | T2 | 19940421 | JP 1992-501019 | 19911212 <-- |
| | US 2001018448 | A1 | 20010830 | US 2001-805474 | 20010313 |
| | US 2002086893 | A1 | 20020704 | US 2001-911906 | 20010724 |
| | US 2003050285 | A1 | 20030313 | US 2002-246872 | 20020919 |
| PRAI | GB 1990-27199 | A | 19901214 | | |
| | WO 1991-GB2226 | A | 19911212 | | |
| | US 1993-74807 | B1 | 19930610 | | |
| | US 1994-304904 | B1 | 19940913 | | |
| | US 1996-614226 | B1 | 19960312 | | |
| | US 1997-775344 | B1 | 19970103 | | |
| | US 1997-940768 | B1 | 19970930 | | |
| | US 1998-153527 | B1 | 19980915 | | |
| | US 1999-272775 | B1 | 19990329 | | |
| | US 2000-603719 | B1 | 20000627 | | |
| | US 2001-805474 | A1 | 20010313 | | |
| | US 2001-911906 | A1 | 20010724 | | |

OS MARPAT 117:205208

AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating hemorrhagic stroke.
 5-Bromo-2-n-butyl-1-(2-chlorophenyl)methyl-1H-benzimidazole-7-carboxylic acid was prepared in 4 steps from 2,5-dibromobenzoic acid. Capsules contain (E)-3-[2-n-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg.

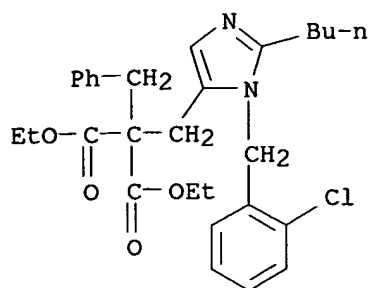
IT 141771-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in angiotensin II receptor antagonist preparation
 for hemorrhagic stroke treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 15 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:605207 CAPLUS

DN 117:205207

TI Use of angiotensin II antagonists in the treatment of angina pectoris

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9210187 | A1 | 19920625 | WO 1991-GB2225 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190816 | A1 | 19920708 | AU 1991-90816 | 19911212 <-- |
| | EP 561979 | A1 | 19930929 | EP 1992-902007 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503323 | T2 | 19940414 | JP 1992-501018 | 19911212 <-- |
| | US 2001016594 | A1 | 20010823 | US 2001-788966 | 20010220 |
| | US 2001051615 | A1 | 20011213 | US 2001-909428 | 20010719 |
| | US 2002058686 | A1 | 20020516 | US 2001-981042 | 20011016 |
| | US 2002132840 | A1 | 20020919 | US 2002-100248 | 20020315 |
| PRAI | GB 1990-27198 | A | 19901214 | | |
| | WO 1991-GB2225 | A | 19911212 | | |
| | US 1994-286158 | B1 | 19940804 | | |
| | US 1996-646175 | B1 | 19960507 | | |
| | US 1997-795843 | B1 | 19970206 | | |
| | US 1998-39656 | B1 | 19980316 | | |
| | US 1999-261893 | B1 | 19990303 | | |
| | US 1999-395833 | B1 | 19990914 | | |
| | US 2000-499864 | B1 | 20000207 | | |
| | US 2000-604450 | A1 | 20000627 | | |
| | US 2001-788966 | A1 | 20010220 | | |
| | US 2001-909428 | A1 | 20010719 | | |
| | US 2001-981042 | A1 | 20011016 | | |

OS MARPAT 117:205207

AB Angiotensin II receptor antagonists (e.g. imidazole derivs.) are used in the manufacture of a medicament for treating angina pectoris. Preparation of 3-[2-n-butyl-1-((2-chlorophenyl)methyl)-1H-imidazol-5-yl]-2-benzylpropanoic acid and 3 other compds. is described. An injection preparation was made from (E)-3-[2-n-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 50 mg in 25 mL normal

saline.

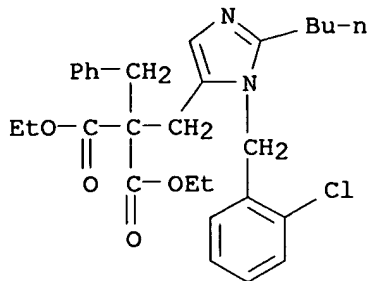
IT **141771-33-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in angiotensin II receptor antagonist preparation for angina treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl)methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 16 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598524 CAPLUS

DN 117:198524

TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists in the treatment of macular degeneration

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9210179 | A1 | 19920625 | WO 1991-GB2217 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190652 | A1 | 19920708 | AU 1991-90652 | 19911212 <-- |
| | EP 561905 | A1 | 19930929 | EP 1992-900761 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503333 | T2 | 19940414 | JP 1992-501726 | 19911212 <-- |
| | US 6025380 | A | 20000215 | US 1999-324330 | 19990602 |
| PRAI | GB 1990-27212 | A | 19901214 | | |
| | WO 1991-GB2217 | A | 19911212 | | |
| | US 1993-74812 | B1 | 19930610 | | |
| | US 1995-375029 | B1 | 19950119 | | |
| | US 1995-535502 | B1 | 19950928 | | |
| | US 1996-724201 | B1 | 19961001 | | |
| | US 1997-901472 | B1 | 19970728 | | |
| | US 1998-170550 | A1 | 19981013 | | |
| OS | MARPAT 117:198524 | | | | |
| AB | Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a | | | | |

medicament for the treatment of macular degeneration. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule contained (E)-3-[2-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

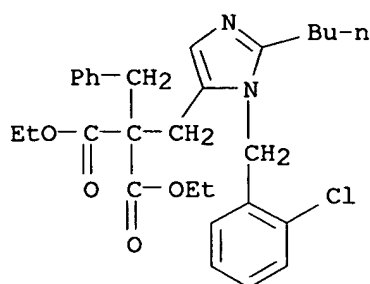
IT **141771-33-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, for angiotensin II antagonist preparation for macular degeneration treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 17 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598523 CAPLUS

DN 117:198523

TI Pharmaceutical compositions, preparation and use of angiotensin II antagonist for the treatment of infarction

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PT | WO 9210180 | A1 | 19920625 | WO 1991-GB2218 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190529 | A1 | 19920708 | AU 1991-90529 | 19911212 <-- |
| | EP 561878 | A1 | 19930929 | EP 1992-900446 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503322 | T2 | 19940414 | JP 1992-501017 | 19911212 <-- |
| | US 2001034360 | A1 | 20011025 | US 2001-847120 | 20010502 |
| | US 2002068759 | A1 | 20020606 | US 2001-21321 | 20011212 |
| | US 2002160985 | A1 | 20021031 | US 2002-134894 | 20020429 |
| | US 2003069293 | A1 | 20030410 | US 2002-271177 | 20021015 |
| PRAI | GB 1990-27208 | A | 19901214 | | |
| | WO 1991-GB2218 | A | 19911212 | | |
| | US 1993-74809 | B1 | 19930610 | | |
| | US 1994-303785 | B1 | 19940909 | | |

US 1995-434144 B1 19950502
 US 1996-588826 B1 19960119
 US 1996-740382 B1 19961029
 US 1997-932418 B1 19970917
 US 1998-158431 B1 19980921
 US 1999-255986 B1 19990223
 US 1999-344782 B1 19990625
 US 1999-431896 B1 19991102
 US 2000-539125 B1 20000330
 US 2000-679149 B1 20001005
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 US 2001-969707 A1 20011003
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 US 2002-134894 A1 20020429

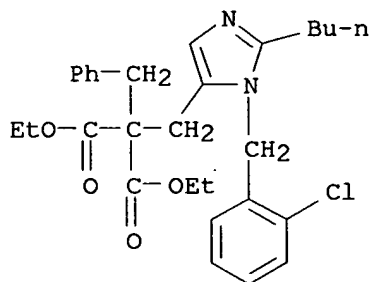
OS MARPAT 117:198523

AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of infarction. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-[(4-carboxyphenyl)methyl]-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

IT **141771-33-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, for angiotensin II antagonist preparation for infarction treatment)

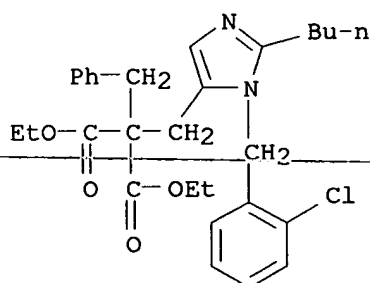
RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 18 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1992:598522 CAPLUS
 DN 117:198522
 TI Pharmaceutical compositions, preparation and use of angiotensin II antagonists in the treatment of left ventricular hypertrophy
 IN Hill, James
 PA Smithkline Beecham PLC, UK
 SO PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|--------|----------|-----------------|--------------|
| PI | WO 9210181 | A1 | 19920625 | WO 1991-GB2219 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190712 | A1 | 19920708 | AU 1991-90712 | 19911212 <-- |
| | JP 06503334 | T2 | 19940414 | JP 1992-501727 | 19911212 <-- |
| | EP 660713 | A1 | 19950705 | EP 1992-900691 | 19911212 <-- |
| | EP 660713 | B1 | 20011024 | | |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | US 6034114 | A | 20000307 | US 1999-371363 | 19990810 |
| PRAI | GB 1990-27209 | A | 19901214 | | |
| | WO 1991-GB2219 | A | 19911212 | | |
| | US 1993-281250 | B1 | 19930330 | | |
| | US 1995-375016 | B1 | 19950119 | | |
| | US 1995-534899 | B1 | 19950928 | | |
| | US 1996-732078 | B1 | 19961016 | | |
| | US 1997-902560 | B1 | 19970728 | | |
| | US 1998-170560 | B1 | 19981013 | | |
| OS | MARPAT 117:198522 | | | | |
| AB | Angiotensin II receptor antagonists (Markush included) are provided for the manufacture of a medicament for the treatment of left ventricular hypertrophy regression. Synthesis of representative compds. is included, and 11 specific compds. are claimed. A capsule formulation contained (E)-3-[2-n-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also presented. | | | | |
| IT | 141771-33-7P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, for angiotensin II antagonist preparation for left ventricular hypertrophy regression treatment) | | | | |
| RN | 141771-33-7 | CAPLUS | | | |
| CN | Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME) | | | | |



L5 ANSWER 19 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:598521 CAPLUS
DN 117:198521
TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists for the prevention of restenosis
IN Hill, James
PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9210185 | A1 | 19920625 | WO 1991-GB2223 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190691 | A1 | 19920708 | AU 1991-90691 | 19911212 <-- |
| | EP 561895 | A1 | 19930929 | EP 1992-900686 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503337 | T2 | 19940414 | JP 1992-501730 | 19911212 <-- |
| | US 5387601 | A | 19950207 | US 1993-74810 | 19930610 <-- |
| PRAI | GB 1990-27200 | A | 19901214 | | |
| | WO 1991-GB2223 | A | 19911212 | | |

OS MARPAT 117:198521

AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the prevention of restenosis after angioplasty or bypass surgery. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

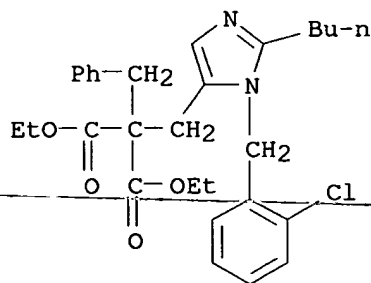
IT 141771-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, for angiotensin II antagonist preparation for restenosis prevention)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598520 CAPLUS

DN 117:198520

TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists for the treatment of atheroma

IN Hill, James

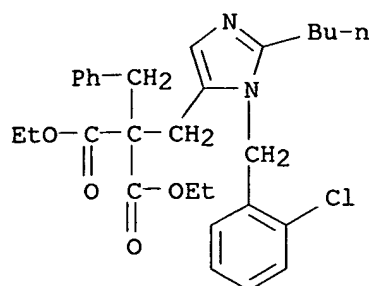
PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9210184 | A1 | 19920625 | WO 1991-GB2222 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190641 | A1 | 19920708 | AU 1991-90641 | 19911212 <-- |
| | EP 561876 | A1 | 19930929 | EP 1992-900436 | 19911212 <-- |
| | EP 561876 | B1 | 19970312 | | |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503336 | T2 | 19940414 | JP 1992-501729 | 19911212 <-- |
| | US 2002006949 | A1 | 20020117 | US 2001-795507 | 20010227 |
| | US 2003004201 | A1 | 20030102 | US 2002-134920 | 20020429 |
| | US 2003166700 | A1 | 20030904 | US 2003-379137 | 20030304 |
| PRAI | GB 1990-27201 | A | 19901214 | | |
| | WO 1991-GB2222 | A | 19911212 | | |
| | US 1994-325731 | B1 | 19941019 | | |
| | US 1995-568919 | B1 | 19951207 | | |
| | US 1997-798671 | B1 | 19970211 | | |
| | US 1997-987288 | B1 | 19971209 | | |
| | US 1998-162404 | B1 | 19980928 | | |
| | US 1999-339303 | B1 | 19990623 | | |
| | US 1999-456870 | B1 | 19991208 | | |
| | US 2000-592492 | A1 | 20000612 | | |
| | US 2001-795507 | B1 | 20010227 | | |
| | US 2001-955398 | A1 | 20010918 | | |
| | US 2002-134920 | B1 | 20020429 | | |
| OS | MARPAT 117:198520 | | | | |
| AB | Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of atheroma. Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given. | | | | |
| IT | 141771-33-7P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, for angiotensin II antagonist preparation for atheroma treatment) | | | | |
| RN | 141771-33-7 CAPLUS | | | | |
| CN | Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME) | | | | |



L5 ANSWER 21 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:598519 CAPLUS

DN 117:198519

TI Pharmaceutical compositions, preparation and use of angiotensin II receptor antagonists in the treatment of diabetic retinopathy

IN Hill, James

PA Smithkline Beecham PLC, UK

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9210183 | A1 | 19920625 | WO 1991-GB2221 | 19911212 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9190649 | A1 | 19920708 | AU 1991-90649 | 19911212 <-- |
| | EP 561901 | A1 | 19930929 | EP 1992-900718 | 19911212 <-- |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 06503335 | T2 | 19940414 | JP 1992-501728 | 19911212 <-- |
| | US 2002128300 | A1 | 20020912 | US 2001-929814 | 20010814 |
| PRAI | GB 1990-27211 | A | 19901214 | | |
| | WO 1991-GB2221 | A | 19911212 | | |
| | US 1993-74869 | B1 | 19930610 | | |
| | US 1994-237461 | B1 | 19940503 | | |
| | US 1995-388781 | B1 | 19950215 | | |
| | US 1996-598760 | B1 | 19960321 | | |
| | US 1997-835693 | B1 | 19970410 | | |
| | US 1998-48708 | B1 | 19980326 | | |
| | US 1999-233689 | B1 | 19990119 | | |
| | US 1999-456867 | B1 | 19991208 | | |
| | US 2000-592492 | A1 | 20000612 | | |
| | US 2000-592495 | B1 | 20000612 | | |
| | US 2001-795021 | A1 | 20010227 | | |

OS MARPAT 117:198519

AB Angiotensin II receptor antagonists, e.g. 2-methyl-4-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methoxy]quinoline, are disclosed for the manufacture of a medicament for the treatment of diabetic retinopathy, Markush are provided, 11 specific compds. are claimed, and preparation of compds. of the invention is described. A capsule formulation contained (E)-3-[2-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5-yl]-2-(2-thienyl)methyl-2-propenoic acid 100, Mg stearate 10, and lactose 100 mg. Tablet and injectable formulations are also given.

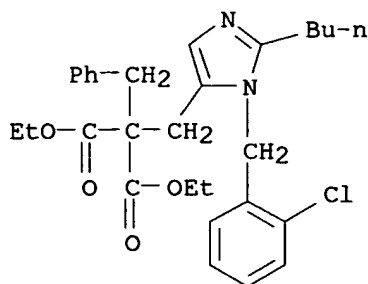
IT 141771-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, for angiotensin II antagonist preparation for diabetic retinopathy treatment)

RN 141771-33-7 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:578319 CAPLUS

DN 117:178319

TI Antihypertensive compositions containing diuretics and angiotensin II receptor antagonists

IN Weinstock, Joseph

PA SmithKline Beckman Corp., USA

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9210097 | A1 | 19920625 | WO 1991-US9362 | 19911213 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | CA 2098176 | AA | 19920614 | CA 1991-2098176 | 19911213 <-- |
| | AU 9191782 | A1 | 19920708 | AU 1991-91782 | 19911213 <-- |
| | AU 656551 | B2 | 19950209 | | |
| | EP 565634 | A1 | 19931020 | EP 1992-904382 | 19911213 <-- |
| | EP 565634 | B1 | 19990317 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE | | | | |
| | JP 06503834 | T2 | 19940428 | JP 1992-504315 | 19911213 <-- |
| | JP 3398379 | B2 | 20030421 | | |
| | AT 177634 | E | 19990415 | AT 1992-904382 | 19911213 |
| | ES 2130170 | T3 | 19990701 | ES 1992-904382 | 19911213 |
| | US 5656650 | A | 19970812 | US 1995-444121 | 19950518 <-- |
| | HK 1012209 | A1 | 20000512 | HK 1998-113489 | 19981215 |
| PRAI | US 1990-628807 | A2 | 19901214 | | |
| | WO 1991-US9362 | A | 19911213 | | |
| | US 1993-75535 | A1 | 19930610 | | |

OS MARPAT 117:178319

AB A pharmaceutical composition contains an angiotensin II receptor antagonist and a compound selected from a diuretic, a Ca channel blocker, a

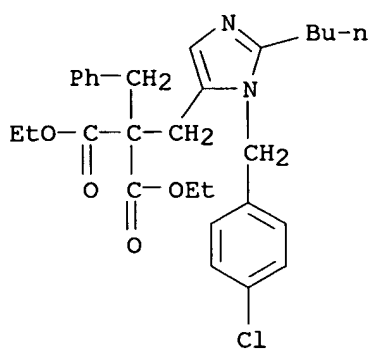
β -adrenoreceptor blocker, a renin inhibitor, and an angiotensin-converting enzyme inhibitor for the treatment of hypertension. A capsule contained (E)-3-[2-butyl-1-[(4-carboxyphenyl)-thienyl]-methyl-2-propenoic acid (I) 100, and hydrochlorothiazide (II) 50mg. II enhanced the hypotensive efficacy of I. Imidazole derivs. (Markush given) as angiotensin II receptor antagonists were prepared

IT **143851-89-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of angiotensin II receptor antagonist)

RN 143851-89-2 CAPLUS

CN Propanedioic acid, [[2-butyl-1-[(4-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 23 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:571061 CAPLUS

DN 117:171061

TI A practical method for the oxidative coupling of aromatic compounds

AU Tanaka, Masahide; Mitsuhashi, Hiroshi; Wakamatsu, Takeshi

CS Tsumura Res. Inst. Biol. Chem., Ami, 300-11, Japan

SO Tetrahedron Letters (1992), 33(29), 4161-4

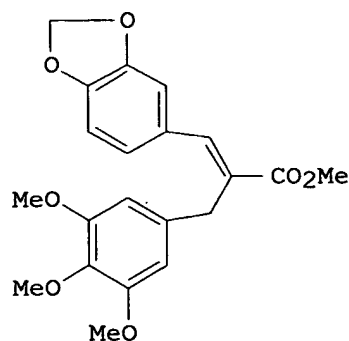
CODEN: TELEAY; ISSN: 0040-4039

DT Journal

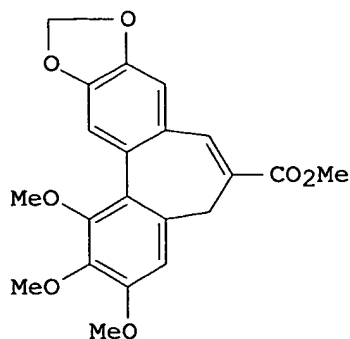
LA English

OS CASREACT 117:171061

GI



I



II

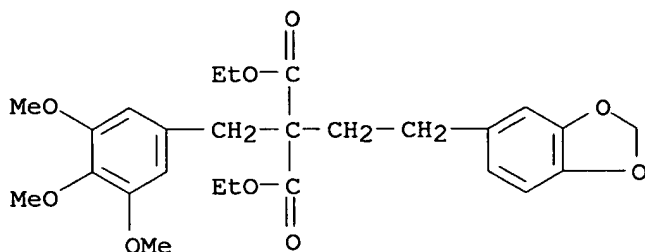
AB A practical method for the oxidative coupling reaction of phenolic and nonphenolic compds. is described. The versatility of this reaction was demonstrated by the successful coupling of the wide variety of substrates including catecholic compds. and known intermediates for the synthesis of steganacin and its analogs. Thus intramol. coupling of diphenylpropene I in the presence of $\text{Fe}(\text{ClO}_4)_3$ in $\text{CF}_3\text{CO}_2\text{H}/\text{CH}_2\text{Cl}_2$ gave 85% dibenzocycloheptene II.

IT 58745-52-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidative coupling reaction of, in the presence of iron perchlorate, dibenzocyclooctane from)

RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 24 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:407921 CAPLUS

DN 117:7921

TI Preparation of imidazolylalkanoates as angiotensin II antagonists

IN Girard, Gerald Robert; Hempel, Judith; Hill, David Taylor; Samanen, James; Weinstock, Joseph

PA SmithKline Beecham Corp., USA

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

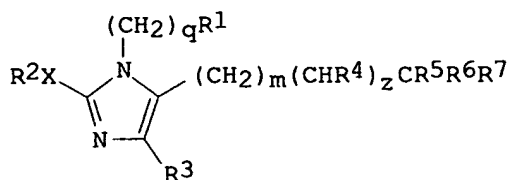
DT Patent

LA English

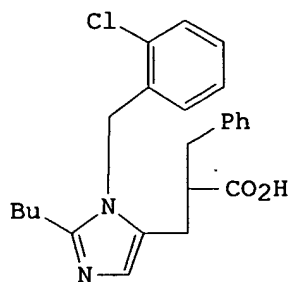
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9202510 | A1 | 19920220 | WO 1991-US5391 | 19910730 <-- |
| | W: AU, CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| | CA 2087840 | AA | 19920201 | CA 1991-2087840 | 19910730 <-- |
| | AU 9184931 | A1 | 19920302 | AU 1991-84931 | 19910730 <-- |
| | AU 649270 | B2 | 19940519 | | |
| | ZA 9105962 | A | 19920729 | ZA 1991-5962 | 19910730 <-- |
| | EP 541705 | A1 | 19930519 | EP 1991-915339 | 19910730 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | JP 05509106 | T2 | 19931216 | JP 1991-514483 | 19910730 <-- |
| | US 5444080 | A | 19950822 | US 1993-965291 | 19930129 <-- |
| | US 5530017 | A | 19960625 | US 1995-433001 | 19950502 <-- |
| PRAI | US 1990-560643 | A2 | 19900731 | | |
| | WO 1991-US5391 | A | 19910730 | | |

US 1993-965291 A3 19930129
 OS MARPAT 117:7921
 GI



I



II

AB Title compds. [I; R1 = adamantylmethyl, (substituted) Ph, biphenyl, naphthyl; R2 = alkyl, alkenyl, alkynyl cycloalkyl, (substituted) Ph; R3 = H, Cl, Br, F, iodo, CHO, HOCH2, CO2R8, NO2, F3C, C2F5, F3CCF2CF2; R4 = H, alkyl; R5 = alkyl, alkenyl, (substituted) phenyl(alkyl), thienyl(alkyl), furyl(alkyl), pyridyl(alkyl), tetrazolyl(alkyl), etc.; R6 = CO2R8, CONR8R8, tetrazol-5-yl; R7 = H, CO2R8, alkyl; R8 = H, alkyl, (methyl)phenyl; X = bond, S, O; m = 0-2; q = 0-4; z = 0-1] are prepared as angiotensin II antagonists (no data). Thus, 2-butyl-1-(2-chlorophenyl)methyl-5-chloromethyl-1H-imidazole (preparation from imidazole given) was condensed with di-Et benzylmalonate using NaH in DMF to give 85% coupling product, which was refluxed with aqueous KOH followed by acidification with HCl to give title compound II. Capsules were prepared containing II.

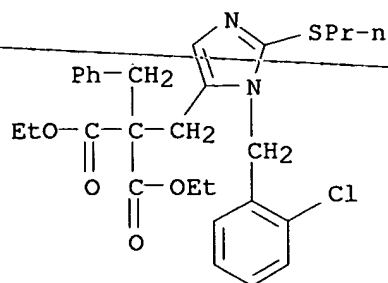
IT 141771-32-6P 141771-33-7P 141771-44-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for imidazolylalkanoate angiotensin II antagonist)

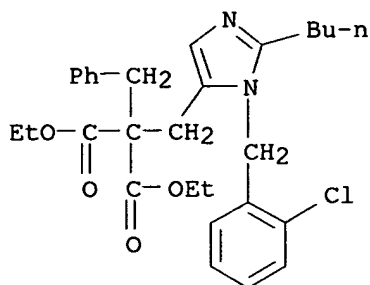
RN 141771-32-6 CAPLUS

CN Propanedioic acid, [[1-[(2-chlorophenyl)methyl]-2-(propylthio)-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)

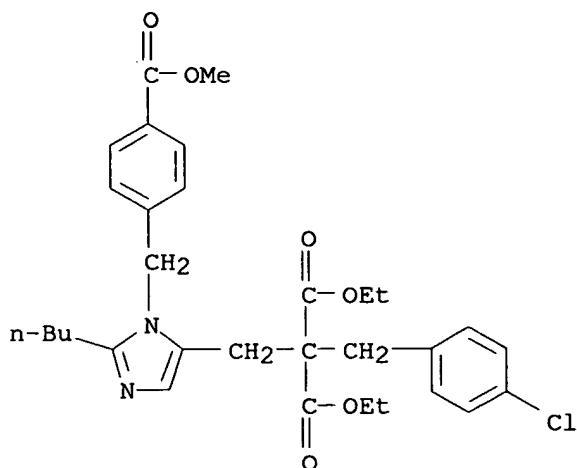


RN 141771-33-7 CAPLUS

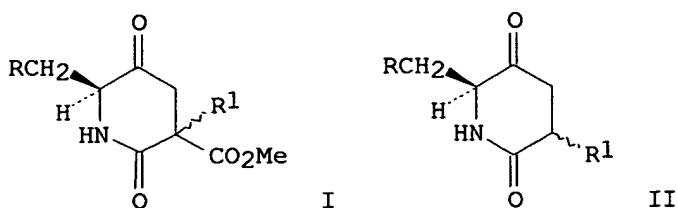
CN Propanedioic acid, [[2-butyl-1-[(2-chlorophenyl)methyl]-1H-imidazol-5-yl]methyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 141771-44-0 CAPLUS
 CN Propanedioic acid, [[2-butyl-1-[[4-(methoxycarbonyl)phenyl]methyl]-1H-imidazol-5-yl]methyl][[(4-chlorophenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 25 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1992:256027 CAPLUS
 DN 116:256027
 TI ~~Synthesis of cyclic ketomethylene dipeptide derivatives~~
 AU Dominguez, M. J.; Gonzalez-Muniz, R.; Garcia-Lopez, M. T.
 CS Inst. Quim. Med., Madrid, 28006, Spain
 SO Tetrahedron (1992), 48(13), 2761-72
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA English
 OS CASREACT 116:256027
 GI



AB Me 6-aralkyl-2,5-diketopiperidine-3-carboxylates I (R = Ph, 3-indolyl; R1 = H) derived from L-Phe and L-Trp, and their 3-substituted analogs I (R = Ph, 3-indolyl; R1 = CH2Ph, CO2CO2Et, Me) in which the 3-substituent is the side chain of Phe, Asp, and Ala have been synthesized. Cyclo[Trpψ(COCH2)Gly] (II; R = 3-indolyl, R1 = H) and cyclo[Pheψ(COCH2)-ξ-Phe] (II; R = Ph, R1 = CH2Ph) have been also prepared

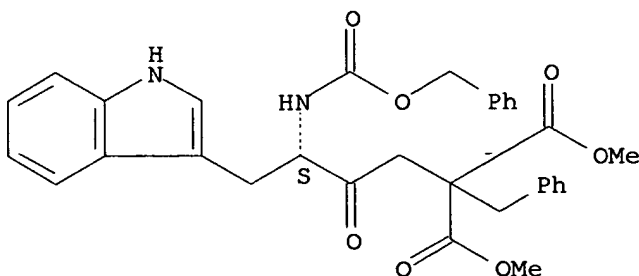
IT 141672-16-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, deblocking, and cyclization of, piperidinedione from)

RN 141672-16-4 CAPLUS

CN Propanedioic acid, [4-(1H-indol-3-yl)-2-oxo-3-[[(phenylmethoxy)carbonyl]amino]butyl] (phenylmethyl)-, dimethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 26 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:56713 CAPLUS

DN 112:56713

TI Preparation of N-acyl-L-histidinamide derivatives as renin inhibitors

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 14 pp.

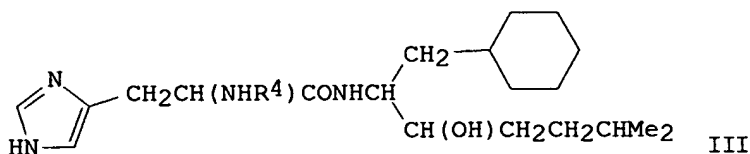
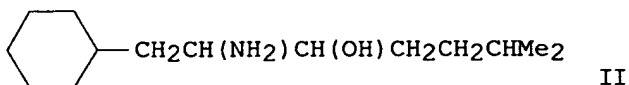
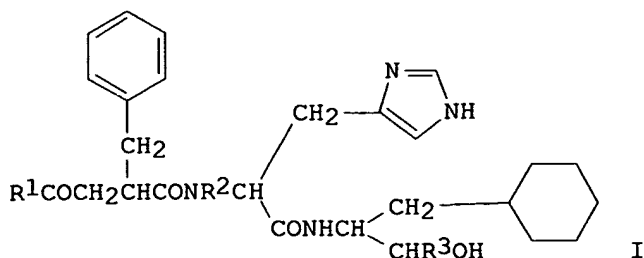
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------------|------|----------|-----------------|--------------|
| PI | JP 01131162 | A2 | 19890524 | JP 1988-259897 | 19881014 <-- |
| PRAI | GB 1987-24428 | A | 19871019 | | |
| OS | MARPAT 112:56713 | | | | |
| GI | | | | | |



AB Amino acid derivs. [I; R1 = (substituted) aryl, alkyl, heterocyclyl; R2 = H, alkyl; R3 = alkyl], effective renin inhibitors useful as antihypertensives, are prepared Ph2P(O)N3 (390 mg) and 144 mg Et3N were added to a solution of 363 mg BOC-His-OH (BOC= tert-BuO2C) and 294 mg (2S,3S)-II in DMF at 0° and stirred overnight at 25° to give 384 mg (2S,3S)-III (R4 = BOC) which was deprotected with CF3CO2H to give 275 mg (2S,3S)-III (R4 = H) (IV). Ph2P(O)N3 (0.75 g) and 0.28 g Et3N were added to a solution of 0.74 g PhCOCH2CH(CO2H)CH2Ph and 1.00 g IV in DMF under ice cooling and the solution stirred overnight at room temperature to give

1.21 g diastereomeric (2S,3S)-I (R1 = Ph, R2 = H, R3 = Me2CHCH2CH2) which was separated by silica gel thin-layer chromatog. Also prepared were 6 addnl. I, 3 of which showed plasma renin inhibitory activity with IC50 of 4.5, 7.9, and 9.5 + 10-8M.

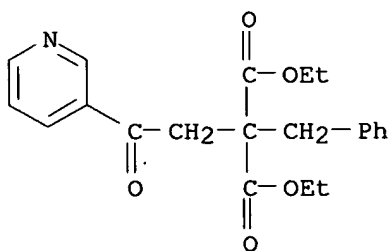
IT **124640-86-4P 124640-89-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

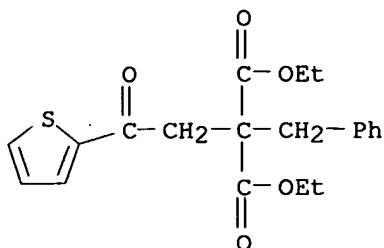
(preparation and reaction of, in preparation of renin inhibitor)

RN 124640-86-4 CAPLUS

CN Propanedioic acid, [2-oxo-2-(3-pyridinyl)ethyl] (phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 124640-89-7 CAPLUS
 CN Propanedioic acid, [2-oxo-2-(2-thienyl)ethyl](phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 27 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1988:94949 CAPLUS
 DN 108:94949
 TI Preparation of statine-containing peptides as orally-active renin inhibitors
 IN Morisawa, Yasuhiro; Yabe, Yuichiro; Kataoka, Mitsuru; Iijama, Yasuteru; Koike, Hiroyuki; Takahagi, Hidekuni; Kokubu, Tatsuo; Hiwada, Kunio
 PA Sankyo Co., Ltd. , Japan
 SO Eur. Pat. Appl., 112 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | EP 228192 | A2 | 19870708 | EP 1986-309362 | 19861201 <-- |
| | EP 228192 | A3 | 19890823 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| | JP 62142145 | A2 | 19870625 | JP 1985-268415 | 19851129 <-- |
| | JP 06062530 | B4 | 19940817 | | |
| | JP 63063649 | A2 | 19880322 | JP 1986-208621 | 19860904 <-- |
| | JP 07020918 | B4 | 19950308 | | |
| | JP 62246546 | A2 | 19871027 | JP 1986-307058 | 19861223 <-- |
| | JP 07049405 | B4 | 19950531 | | |
| PRAI | JP 1985-268415 | A | 19851129 | | |
| | JP 1985-297664 | A | 19851226 | | |
| | JP 1986-208621 | A | 19860904 | | |

OS CASREACT 108:94949

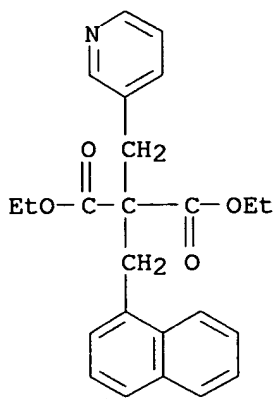
AB R1R2CHCONR3CHR4CONHCH(CH2R5)CH(OH)(CH2)nCONH(CHR6CONH)nR7 [I; R1 = arylalkyl, heterocyclylalkyl, acylalkyl, alkoxyalkoxyalkyl, (substituted) carbamoyl, acylamino; R2 = arylalkyl, heterocyclylalkyl; R3 = H, alkyl; R4 = H, (substituted) alkyl, haloalkenyl, alkynyl, cycloalkyl; R5 = Me2CH, cycloalkyl, Ph; R6 = alkyl; R7 = (substituted) alkyl; m, n = 0, 1] were prepared as renin inhibitors. N-Nicotinoyl-3-(1-naphthyl)-L-alanyl-L-leucylstatyl-L-lysinoil.HCl was prepared via solution-phase method using (EtO)2P(O)CN/Et3N in DMF. I gave 68-98% inhibition of human renin at 10-6M.

IT 112804-18-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as renin inhibitor intermediate)

RN 112804-18-9 CAPLUS

CN Propanedioic acid, (1-naphthalenylmethyl)(3-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 28 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:617788 CAPLUS

DN 107:217788

TI Acetyl substitution of the cyclopentadienyl ligand in molybdenum complexes; nucleophilic additions to coordinated allyl groups

AU Vanarsdale, W. E.; Kochi, J. K.

CS Dep. Chem., Univ. Houston, Houston, TX, 77004, USA

SO Journal of Organometallic Chemistry (1986), 317(2), 215-32

CODEN: JORCAI; ISSN: 0022-328X

DT Journal

LA English

OS CASREACT 107:217788

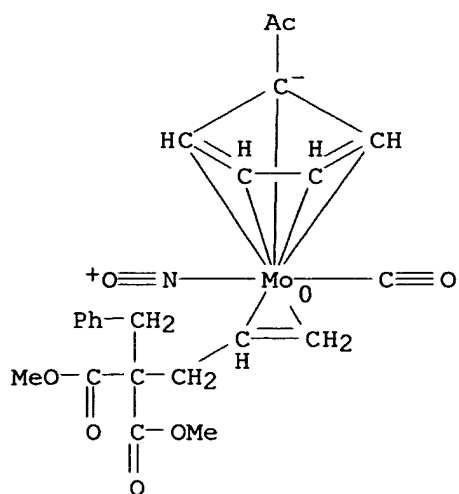
AB Reaction of $\text{CpMoL}(\text{CO})_2(\text{NCMe})_2$ (I; L = η^3 -allyl, η^3 - CH_2CHCHMe , η^3 - CHCMeCH_2) with CpLi (Cp = η^5 -cyclopentadienyl) gave $\text{CpMoL}(\text{CO})_2$ (same L) and <10% $(\text{AcCp})\text{MoL}(\text{CO})_2$ (II). II (same L) were also prepared in 50-60% yields by treating I with lithiated acetylcyclopentadiene. The origin of the Ac group was determined by D labeling, and is rationalized in terms of activation of the coordinated MeCN to nucleophilic addition with CpLi . The x-ray crystal structure of II (L = η^3 -allyl) showed a slightly distorted Cp ring and an effective enlargement of the ligand as a result of Ac substitution. Stereoelectronic consequences of the AcCp ligand are found in the relative populations of the exo and endo conformations of the coordinated allyl ligands in both II and $(\text{AcCp})\text{Mo}(\text{CO})(\text{NO})(\eta^3\text{-allyl})^+$ (III) by comparison with their unsubstituted analogs. The stereochem. resulting from this steric change is also examined in nucleophilic addns. to III with H^- , thiolate anions, and carbanions.

IT 111194-27-5P

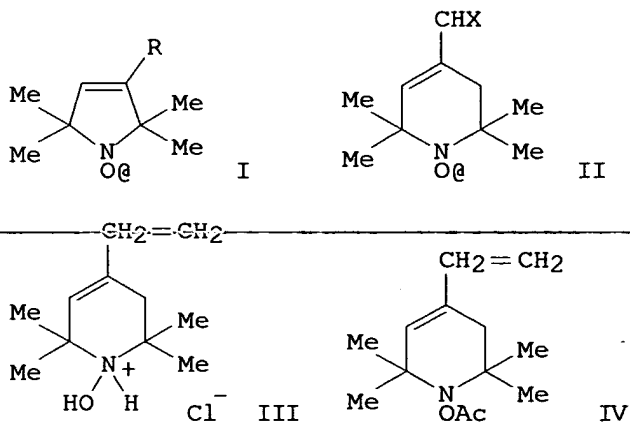
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation and rotamers of)

RN 111194-27-5 CAPLUS

CN Molybdenum, [(1,2,3,4,5- η)-1-acetyl-2,4-cyclopentadien-1-yl]carbonyl[dimethyl (phenylmethyl)][(2,3- η)-2-propenyl]propanedioate]nitrosyl- (9CI) (CA INDEX NAME)



L5 ANSWER 29 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1987:423206 CAPLUS
 DN 107:23206
 TI Further syntheses with nitroxide α,β -unsaturated aldehydes and allylic bromides
 AU Hideg, Kalman; Cseko, Jozsef; Hankovszky, H. Olga; Sohar, Pal
 CS Cent. Lab. Chem., Univ. Pecs, Pecs, H-7643, Hung.
 SO Canadian Journal of Chemistry (1986), 64(8), 1482-90
 CODEN: CJCHAG; ISSN: 0008-4042
 DT Journal
 LA English
 OS CASREACT 107:23206
 GI



AB The enhanced reactivity of nitroxide allylic bromides, e.g. I ($R = \text{CH}_2\text{Br}$), is used for preparation of spin-labeled analogs of biol. active compds. (morphine, Nalorphine, barbituric acid, choline and acetyl choline). Thus, I ($R = \text{CH}_2\text{Br}$) was treated with $\text{Me}_2\text{NCH}_2\text{CH}_2\text{OAc}$ to give 45% I ($R =$

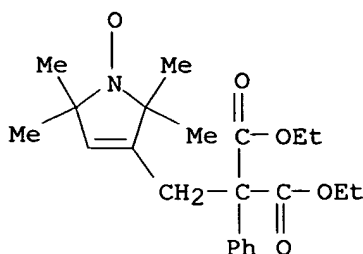
CH₂N+Me₂CH₂CH₂OAc Br-). Nitroxide α,β -unsatd. aldehydes, e.g. II (X = O), are reacted with phosphoranes to give nitroxide polyenes, e.g. II (X = CH₂). The nitroxides are reduced to diamagnetic N-hydroxy hydrochloride salts, e.g. III, which can be converted in the presence of base to N-acetoxy derivs., e.g. IV.

IT 105843-26-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 105843-26-3 CAPLUS

CN 1H-Pyrrol-1-yloxy, 3-[3-ethoxy-2-(ethoxycarbonyl)-3-oxo-2-phenylpropyl]-
2,5-dihydro-2,2,5,5-tetramethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:19056 CAPLUS

DN 106:19056

TI 5-Amino-4-hydroxyvaleramide derivatives.

IN Buehlmayer, Peter; Rasetti, Vittorio; Fuhrer, Walter; Stanton, James
Lawrence; Goeschke, Richard

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 180 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| PI | EP 184550 | A2 | 19860611 | EP 1985-810523 | 19851108 <-- |
| | EP 184550 | A3 | 19880120 | | |
| | EP 184550 | B1 | 19920318 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | US 4727060 | A | 19880223 | US 1985-794914 | 19851104 <-- |
| | AT 73778 | E | 19920415 | AT 1985-810523 | 19851108 <-- |
| | FI 8504434 | A | 19860514 | FI 1985-4434 | 19851111 <-- |
| | DD 239210 | A5 | 19860917 | DD 1985-282727 | 19851111 <-- |
| | DK 8505202 | A | 19860514 | DK 1985-5202 | 19851112 <-- |
| | NO 8504516 | A | 19860514 | NO 1985-4516 | 19851112 <-- |
| | AU 8549821 | A1 | 19860522 | AU 1985-49821 | 19851112 <-- |
| | AU 592768 | B2 | 19900125 | | |
| | JP 61122296 | A2 | 19860610 | JP 1985-252104 | 19851112 <-- |
| | ZA 8508662 | A | 19860730 | ZA 1985-8662 | 19851112 <-- |
| | HU 39193 | A2 | 19860828 | HU 1985-4327 | 19851112 <-- |
| | ES 548798 | A1 | 19870501 | ES 1985-548798 | 19851112 <-- |
| | ES 557316 | A1 | 19880401 | ES 1987-557316 | 19870114 <-- |
| | US 4931591 | A | 19900605 | US 1989-380711 | 19890712 <-- |
| | AU 8943855 | A1 | 19900322 | AU 1989-43855 | 19891027 <-- |

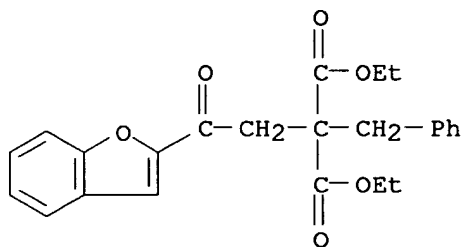
PRAI CH 1984-5426 A 19841113
 CH 1985-3094 A 19850717
 CH 1983-6285 A 19831123
 US 1985-794914 A3 19851104
 EP 1985-810523 A 19851108
 US 1987-123618 B1 19871228

AB R1-Z-NR2CHR3CHR4CH2CHR5COR6 I [R1 = H, acyl; R2 = H, alkyl; R3 = H, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R4 = OH, etherified or OH, acyloxy; R5 = alkyl, etherified hydroxyalkyl, acyloxyalkyl, cycloalkyl, etc.; R6 = substituted amino; Z = (N-alkyl) α -amino acid residue], useful as antihypertensives and cardiac stimulants (no data), were prepared Thus, N-(2-quinolylcarbonyl)-L-phenylalanine was condensed with Me₂CHCH₂CH(NH₂)CH(OH)CH₂CH(CHMe₂)CONHMe in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide to give I [R1 = 2-quinolylcarbonyl, R2 = H, R3 = Me₂CHCH₂, R4 = OH, R5 = CHMe₂, R6 = NHMe, Z = Phe]. Gelatin solns. were prepared from N-[2-(R, S)-benzyl-5,5-dimethyl-4-oxohexanoyl]-His-Cha-cVal-NHBu [Cha = reduced L-cyclohexylalanyl, cVal = CH₂CH(CHMe₂)CO] 3 mg, gelatin 150.0 mg, phenol 4.7 mg, and water (to 1.0 mL total volume).

IT **105852-56-0P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of)

RN 105852-56-0 CAPLUS

CN Propanedioic acid, [2-(2-benzofuranyl)-2-oxoethyl] (phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 31 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1986:149076 CAPLUS
 DN 104:149076
 TI Stereoselectivity in carbanion addition to coordinated allyl ligands.
~~Catalytic (exo-endo) isomerization of cationic molybdenum complexes~~
 AU VanArsdale, W. E.; Winter, R. E. K.; Kochi, J. K.
 CS Dep. Chem., Univ. Houston, Houston, TX, 77004, USA
 SO Organometallics (1986), 5(4), 645-55
 CODEN: ORGND7; ISSN: 0276-7333
 DT Journal
 LA English
 OS CASREACT 104:149076
 AB Regio- and stereochem. in the nucleophilic addition of various types of carbanions to coordinated allyl ligands is examined in a series of (η^5 -C₅H₅)Mo(NO)(CO)(η^3 -allyl)⁺ (I). Stereoselectivity is determined primarily by the conformational preference of the allyl ligand in the endo and exo isomers of I. Different additives, including the carbanion itself, induce an efficient catalytic equilibration of the conformational

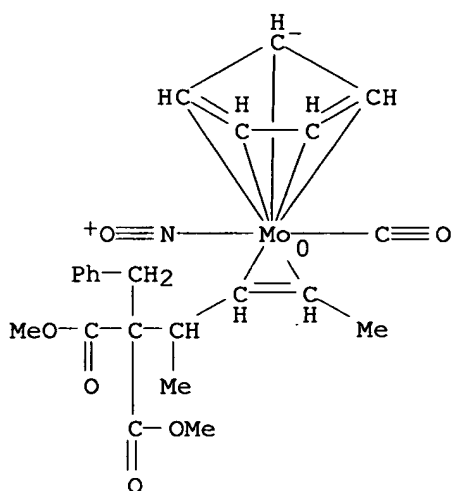
population which can be faster than nucleophilic addition. The rapidity of such a preequil. endo-exo interconversion can lead to a high degree of stereoselectivity in the addition of various carbanionic nucleophiles to I. Thus the η^2 -olefin product of the addition of the di-Me benzylmalonate anion to the 1,3-dimethallyl cation is a single diastereomer formed in high yields. The stereochem. of the adduct $(\eta^5\text{-C}_5\text{H}_5)\text{Mo}(\text{NO})(\text{CO})(\eta^2\text{-C}_{17}\text{H}_{22}\text{O}_4)$ is established by x-ray crystallog.

IT **100243-60-5P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)

RN 100243-60-5 CAPLUS

CN Molybdenum, carbonyl(η^5 -2,4-cyclopentadien-1-yl)[dimethyl
[(2,3- η)-1-methyl-2-butenyl](phenylmethyl)propanedioate]nitrosyl-,
stereoisomer (9CI) (CA INDEX NAME)

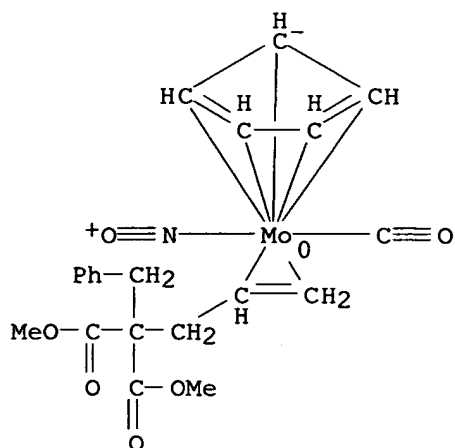


IT **100229-44-5P**

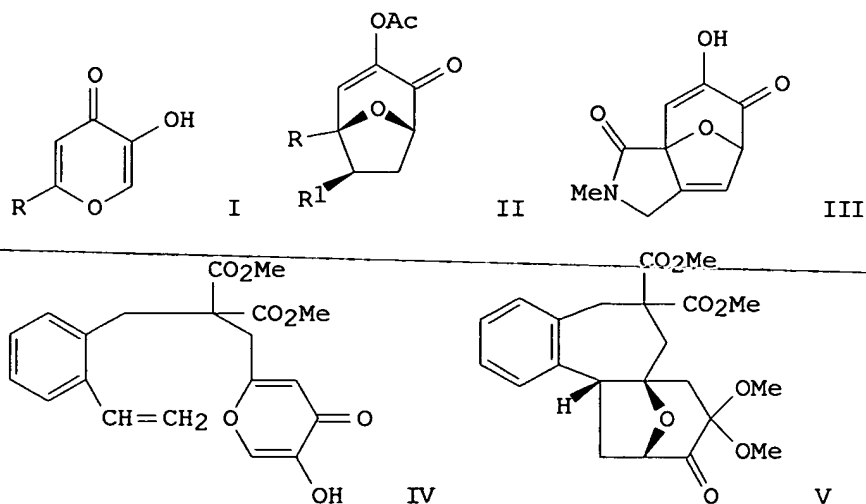
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 100229-44-5 CAPLUS

CN Molybdenum, carbonyl(η^5 -2,4-cyclopentadien-1-yl)[dimethyl
(phenylmethyl)[(2,3- η)-2-propenyl]propanedioate]nitrosyl-,
stereoisomer (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1983:522228 CAPLUS
 DN 99:122228
 TI Intramolecular cycloadditions with 2-(ω -alkenyl)-5-hydroxy-4-pyrones
 AU Garst, Michael E.; McBride, Bill J.; Douglass, James G., III
 CS Dep. Chem., Univ. California, San Diego, CA, 92093, USA
 SO Tetrahedron Letters (1983), 24(16), 1675-8
 CODEN: TELEAY; ISSN: 0040-4039
 DT Journal
 LA English
 OS CASREACT 99:122228
 GI



AB The intramol. cycloaddn. reaction of the pyrones I [R = CONMeCH₂CH:CH₂, CH₂C(CO₂Me)₂(CH₂)_nCH:CH₂ (n = 1, 2)] in refluxing C₆H₆ for 12-48 h followed by acetylation gave the tricyclic compds. II [RR1 = CONHMeCH₂,

$\text{CH}_2\text{C}(\text{CO}_2\text{Me})_2(\text{CH}_2)_n$ ($n = 1, 2$), resp., in 55-70% yield. Similarly, cycloaddn. reaction of I ($\text{R} = \text{CONMeCH}_2\text{C.tplbond.CH}$) gave 42% tricyclic compound III. Treatment of pyrone IV with MeSO_3H in refluxing MeOH for 12 h gave 87% ketal V.

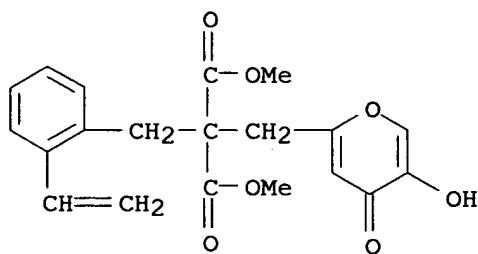
IT 87057-53-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, intramol. cycloaddn. reaction, and ketalization of)

RN 87057-53-2 CAPLUS

CN Propanedioic acid, [(2-ethenylphenyl)methyl][(5-hydroxy-4-oxo-4H-pyran-2-yl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 33 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1981:139754 CAPLUS

DN 94:139754

TI Synthesis of some pyrazolo [diazepine, pyrazole, isoxazole and pyrimidine] derivatives and related compounds

AU Afsah, El Sayed; Amer, Fathy A.; Soafan, Momdough

CS Fac. Sci., Mansoura Univ., Mansoura, Egypt

SO Zeitschrift fuer Naturforschung, Teil B: Anorganische Chemie, Organische Chemie (1980), 35B(10), 1313-16

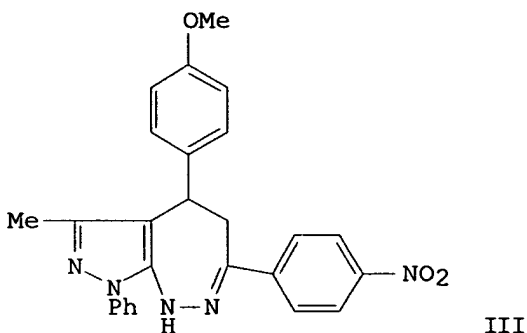
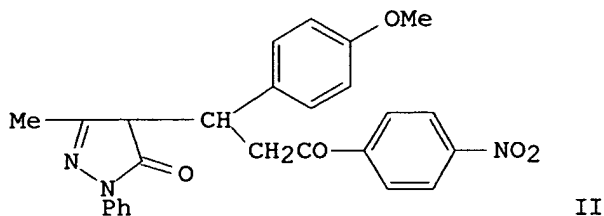
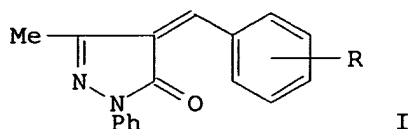
CODEN: ZNBAD2; ISSN: 0340-5087

DT Journal

LA English

OS CASREACT 94:139754

GI



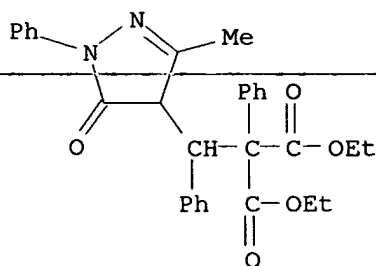
AB Eighteen title compds. were prepared in 55-75% yields by various methods starting from I (R = H, o-, p-OH, p-MeO). Thus, Michael condensation of I (R = p-MeO) with p-O₂NC₆H₄Ac gave 75% II, which on cyclization with NH₂NH₂ gave 60% III.

IT **76794-82-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 76794-82-6 CAPLUS

CN Propanedioic acid, [(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)phenylmethyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



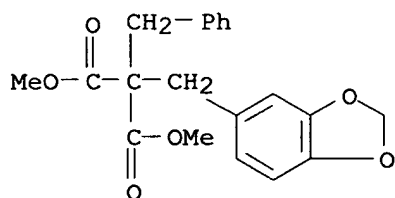
L5 ANSWER 34 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1980:471212 CAPLUS

DN 93:71212

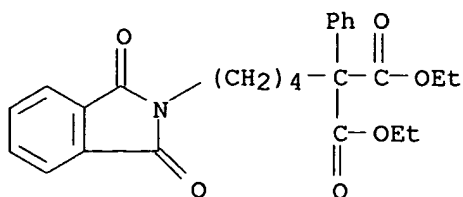
TI Dependence of aryl ether acylation upon Lewis acid stoichiometry

AU Buckley, Thomas F., III; Rapoport, Henry
 CS Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
 SO Journal of the American Chemical Society (1980), 102(9), 3056-62
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 OS CASREACT 93:71212
 AB Acylation of alkyl aryl ethers depends on the stoichiometry of the Friedel-Crafts catalyst. With 100 mol% catalyst, acylation proceeds rapidly and in high yield; with large molar excesses of catalyst, the reaction is essentially completely arrested. This inhibition can be reversed by using sterically bulky alkyl groups, which effectively prevent complexing between catalyst and aryl ether. Based on these observations, processes were developed for regioselective intramol. acylation of either a Ph or an alkoxyated Ph ring when both are present.
 IT **74402-07-6P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrolysis-decarboxylation of)
 RN 74402-07-6 CAPLUS
 CN Propanedioic acid, (1,3-benzodioxol-5-ylmethyl)(phenylmethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 35 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1980:460855 CAPLUS
 DN 93:60855
 TI Phenobarbital specific antibody production: preparation
 5-phenyl-5-(4-aminobutyl) barbituric acid-bovine serum albumin conjugate
 AU Castro, Albert; Chung, Alfred; Monji, Nobuo
 CS Sch. Med., Univ. Miami, Miami, FL, 33101, USA
 SO Research Communications in Chemical Pathology and Pharmacology (1980), 28(2), 309-17
~~CODEN: RCOCB8; ISSN: 0034-5164~~
 DT Journal
 LA English
 AB The aminobutyl derivative of phenobarbital, 5-phenyl-5-(4-aminobutyl)barbituric acid hydrochloride [42240-88-0] was synthesized through two synthetic pathways for the preparation of immunogen in production of phenobarbital [50-06-6] specific antibody. The produced antiserum had high titer, specificity, affinity, and sensitivity (0.5 ng/mL), when examined by radioimmunoassay.
 IT **74385-16-3P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, with urea)
 RN 74385-16-3 CAPLUS

CN Propanedioic acid, [4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)butyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 36 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1979:87434 CAPLUS

DN 90:87434

TI Total synthesis of (±)-picropodophyllone and (±)-4'-demethylpicropodophyllone

IN Kende, Andrew S.

PA University of Rochester, USA

SO U.S., 8 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 4122092 | A | 19781024 | US 1977-827487 | 19770825 <-- |
| | CA 1088952 | A1 | 19801104 | CA 1978-309690 | 19780821 <-- |
| | GB 2003152 | A | 19790307 | GB 1978-34349 | 19780823 <-- |
| | GB 2003152 | B2 | 19820120 | | |
| | GB 2017695 | A | 19791010 | GB 1979-10536 | 19780823 <-- |
| | GB 2017695 | B2 | 19820120 | | |
| | CH 636870 | A | 19830630 | CH 1978-8927 | 19780823 <-- |
| | DE 2837033 | A1 | 19790322 | DE 1978-2837033 | 19780824 <-- |
| | DE 2837033 | C2 | 19880421 | | |
| | JP 54095572 | A2 | 19790728 | JP 1978-102367 | 19780824 <-- |
| | JP 61025033 | B4 | 19860613 | | |
| | ES 472864 | A1 | 19791016 | ES 1978-472864 | 19780825 <-- |
| PRAI | US 1977-827487 | A | 19770825 | | |
| GI | | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Methylenedioxytetralonedicarboxylates I (R = alkyl, R1 = H), intermediates in synthesis of the title compds., were prepared by cyclization of benzodioxoles II with Tl(OAc)3. Thus, II (R = Et, R1 = Me) was cyclized with Tl(OAc)3 to give I (R = Et, R1 = Me), which was oxidized followed by hydrolysis-decarboxylation and cyclization with HCHO to give (±)-3-hydroxymethylpicropodophyllone, which was treated with Jones reagent to give (±)-picropodophyllone (III).

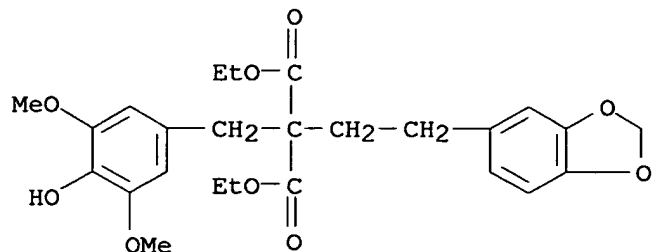
IT 66655-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cyclization of)

RN 66655-29-6 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(4-hydroxy-3,5-dimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 37 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1978:424198 CAPLUS

DN 89:24198

TI Product control in oxidative aryl-benzyl coupling of a phenolic 1,4-diarylbutane

AU Kende, Andrew S.; Rutledge, P. Stewart

CS Dep. Chem., Univ. Rochester, Rochester, NY, USA

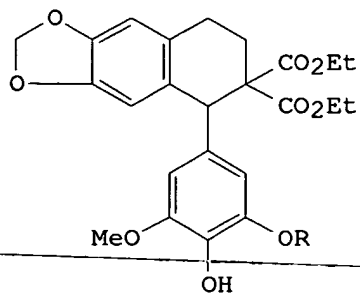
SO Synthetic Communications (1978), 8(4), 245-50

CODEN: SYNCAV; ISSN: 0039-7911

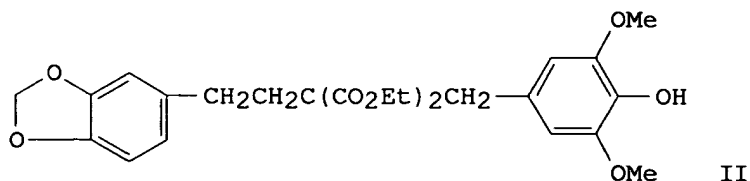
DT Journal

LA English

GI



I



II

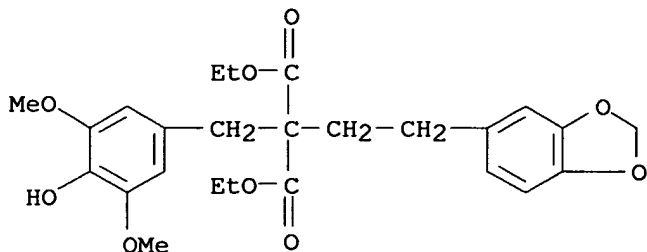
AB Naphthodioxole I (R = H) was prepared in 66% yield by cyclization of II in presence of Tl(O2CCF3)2. Addnl. obtained was 55% I (R = Me).

IT 66655-29-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, by thallium bis(trifluoroacetate))

RN 66655-29-6 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(4-hydroxy-3,5-dimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 38 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1978:120902 CAPLUS

DN 88:120902

TI Synthetic studies on lignan lactones: aryl dithiane route to
(±)-podorhizol and (±)-isopodophyllotoxone and approaches to the
stegane skeleton

AU Ziegler, Frederick E.; Schwartz, John A.

CS Sterling Chem. Lab., Yale Univ., New Haven, CT, USA

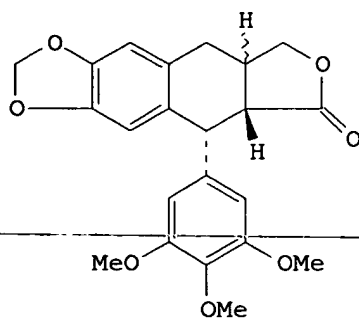
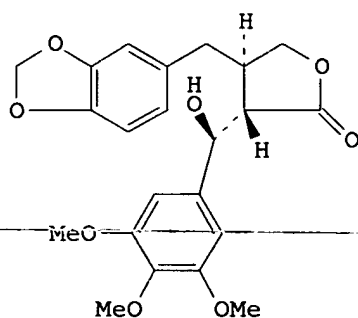
SO Journal of Organic Chemistry (1978), 43(5), 985-91

CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA English

GI



AB The conjugate addition of aryl dithiane anions to 2-butenolide was discussed. The results of the trapping of the resultant lactone enolates with an aryl halide and aryl aldehyde are detailed. The transformation of these intermediates into podorhizol (I) and isopodophyllotoxone II was also explored. The structures of products from attempted intramol. Ullmann couplings in the stegane series were established.

IT 64490-60-4P

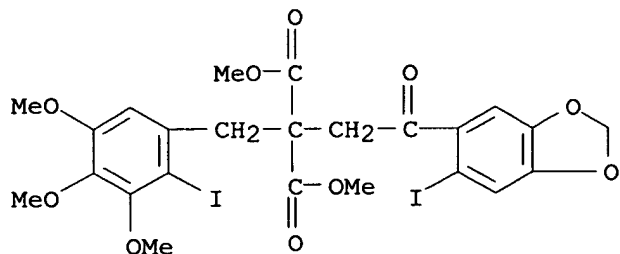
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation and reaction of, with cuprous complexes)

RN 64490-60-4 CAPLUS

CN Propanedioic acid, [2-(6-iodo-1,3-benzodioxol-5-yl)-2-oxoethyl][(2-iodo-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI) (CA INDEX NAME)



IT 64521-00-2P 64521-01-3P

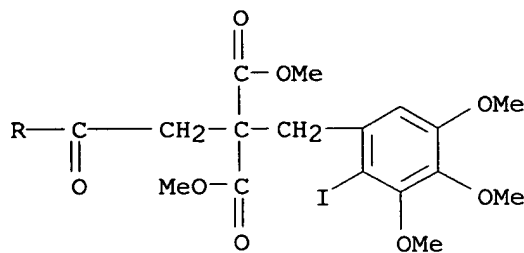
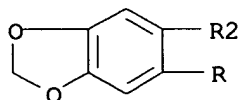
RL: SPN (Synthetic preparation); PREP (Preparation)

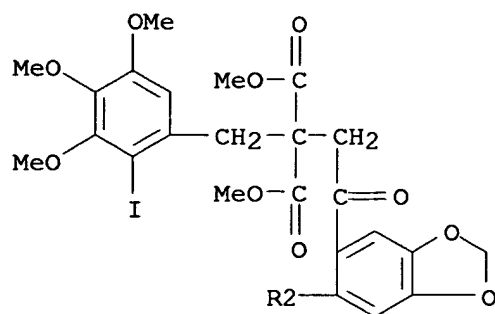
(preparation of)

RN 64521-00-2 CAPLUS

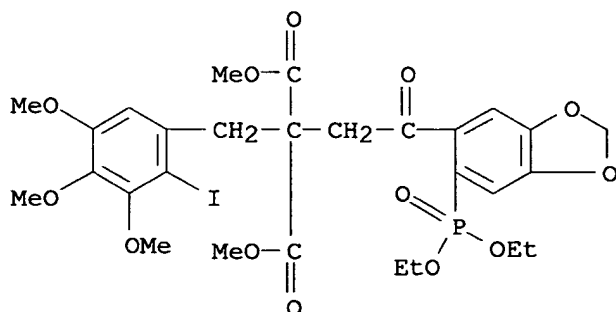
CN [5,5'-Bi-1,3-benzodioxole]-6,6'-dibutanoic acid, α,α' -bis[(2-iodo-3,4,5-trimethoxyphenyl)methyl]- α,α' -bis(methoxycarbonyl)- γ,γ' -dioxo-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

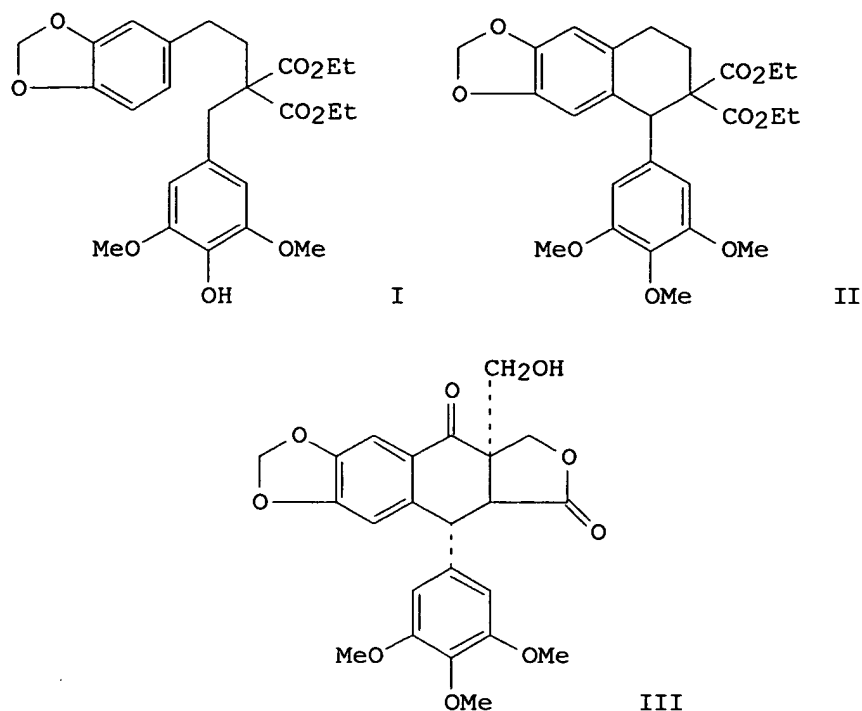




RN 64521-01-3 CAPLUS
 CN Propanedioic acid, [2-[6-(diethoxyphosphinyl)-1,3-benzodioxol-5-yl]-2-oxoethyl][(2-iodo-3,4,5-trimethoxyphenyl)methyl]-, dimethyl ester (9CI)
 (CA INDEX NAME)



L5 ANSWER 39 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1978:6782 CAPLUS
 DN 88:6782
 TI Oxidative aryl-benzyl coupling. A biomimetic entry to podophyllin lignan lactones
 AU Kende, Andrew S.; Liebeskind, Lanny S.; Mills, John E.; Rutledge, P. Stewart; Curran, Dennis P.
 CS Dep. Chem., Univ. Rochester, Rochester, NY, USA
 SO ~~Journal of the American Chemical Society (1977), 99(21), 7082-3~~
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 GI



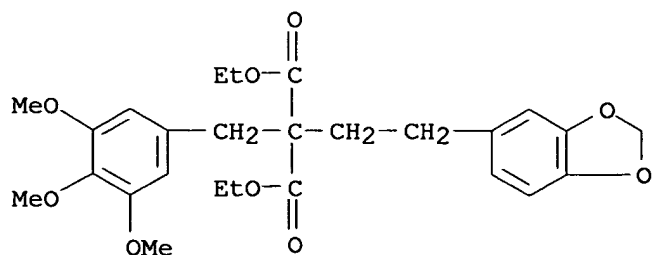
AB Thallium(III) trifluoroacetate oxidation of the phenolic 1,4-diarylbutane I leads to the formation of the 1-aryltetralin ring system characteristic of podophyllin lignan lactones. The tricyclic diester II obtained from I after reductive workup and methylation can be oxidized to the C-4 ketone in one step in 90% yield. Hydrolysis, decarboxylation and reaction with HCHO and base yields the hydroxylactone III, which on thermal or oxidative retroaldolization gives (\pm)-picropodophyllone (IV) in 13% overall yield from I. The probable role of o-quinone in the oxidative cyclization of I is discussed.

IT **58745-52-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)

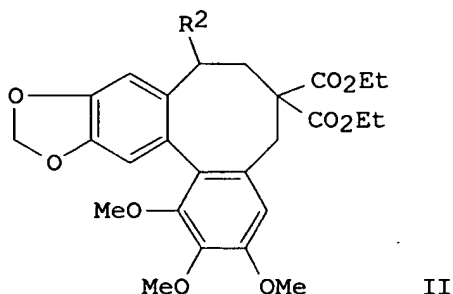
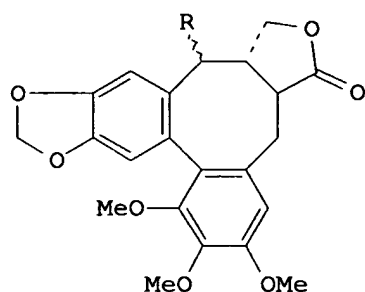
RN 58745-52-1 CAPLUS

CN ~~Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)~~



L5 ANSWER 40 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1977:189909 CAPLUS
 DN 86:189909
 TI Total synthesis of steganacin and derivatives
 IN Kende, Andrew S.; Liebeskind, Lanny S.
 PA USA
 SO U.S., 22 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 4003916 | A | 19770118 | US 1975-642954 | 19751222 <-- |
| PRAI | US 1975-642954 | A | 19751222 | | |
| GI | | | | | |



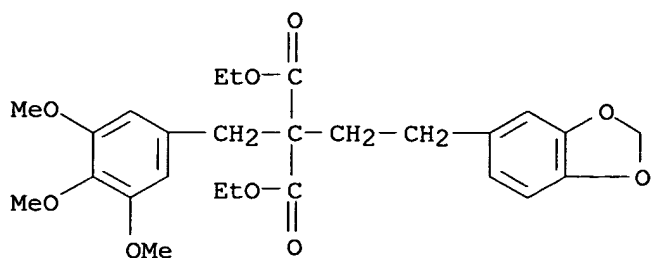
AB The title compds. (I, R = α -OH, β -OH, β -OAc) were prepared by mesylating homopiperonyl alc. (R1OH), treating R1O3SMe with CH(CO2Et)2, treating R1CH(CO2Et)2 with 3,4,5-(MeO)3C6H2CH2Br, cyclizing R1C(CO2Et)2CH2C6H2(OMe)3-3,4,5, oxidizing II (R2 = H) with benzoyl peroxide, oxidizing II (R2 = OH) with Jones reagent, decarboxylating the ketone, cyclizing the monoester with CH2O, and reducing with NaBH4 to give I (R = α -OH, β -OH). I (R = β -OH) was esterified to I (R = β -OAc, β -O2CCMe:CHMe).

IT 58745-52-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclization of)

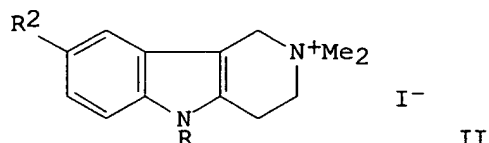
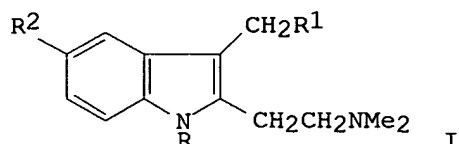
RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 41 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1976:150497 CAPLUS
 DN 84:150497
 TI 3-Substituted isotryptamine derivatives
 IN Zinnes, Harold; Schwartz, Martin L.
 PA Warner-Lambert Co., USA
 SO U.S., 9 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 3931230 | A | 19760106 | US 1974-460397 | 19740412 <-- |
| PRAI | US 1974-460397 | A | 19740412 | | |
| GI | | | | | |



AB Eighteen isotryptamines I [R = R2 = H, R1 = cyano, 4,4-dimethyl-2,6-dioxocyclohexyl, CMe2NO2, CH(SO2Ph)2, CH(CO2Me)2, CR3(CO2Et)2 (R3 = Me, Ph, NHAc), 2-oxo-1-phenylcyclohexyl, CPh2CN, CPh2Ac, P(O)(OEt)2, CSNMe2, SO2Ph; R = Me, R1 = CMe2NO2, cyano, R2 = H; R = H, R1 = CMe(CO2Et)2, R2 = MeO, Br] or their HCl salts were prepared by reaction of γ -carboline II with an anion (R1)-. The anion was used as the com. available Na-salt (e.g., NaCN) or prepared in situ by treatment of the conjugate acid with a base. I [R = Me; R1 = cyano, CPh2CN, 2-oxo-1-phenylcyclohexyl, CMe(CO2Et)2; R2 = H] were prepared by methylation (MeI) of I (R = H, R1 and R2 as above). I (R = H, Me; R1 = CONH2, R2 = H) was prepared by aqueous hydrolysis of I (R1 = cyano), I (R = R2 = H, R1 = CO2Et.HCl) by treating I (R1 = cyano) with HCl in EtOH, and I (R = Me, R1 = CPh2H, R2 = H) and its HCl salt by refluxing I (R1 = CPh2CN, R and R2 as above) with MeLi 20 hr in C6H6. I are useful as sedatives and antiaggression agents (no data).

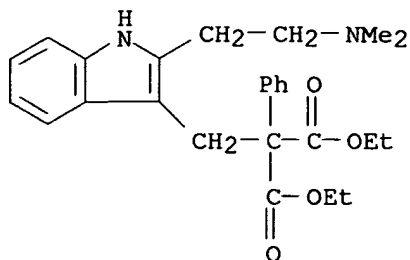
IT **58981-74-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 58981-74-1 CAPLUS

CN Propanedioic acid, [[2-[2-(dimethylamino)ethyl]-1H-indol-3-

yl]methyl]phenyl-, diethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

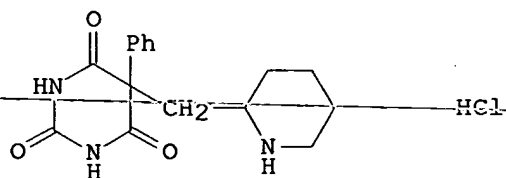


● HCl

L5 ANSWER 42 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1976:140749 CAPLUS
 DN 84:140749
 TI Antiparkinsonism compositions
 IN Wiggins, Leslie F.; James, John William; Gittos, Maurice W.
 PA Aspro-Nicholas Ltd., UK
 SO U.S., 16 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 3930006 | A | 19751230 | US 1965-510108 | 19650722 <-- |
| | US 3857844 | A | 19741231 | US 1966-526707 | 19660211 <-- |
| PRAI | US 1960-75911 | A2 | 19601215 | | |
| | US 1963-276977 | A3 | 19630430 | | |
| | US 1963-277431 | A2 | 19630502 | | |

GI



I

AB Barbituric and thiobarbituric acid derivs. useful for ameliorating symptoms of paralysis agitans associated with Parkinsonism are reported. 5-Phenyl-5-(2-piperidinylmethyl)barbituric acid-HCl (I) [20432-72-8], the preferred compound of the invention, compared favorably with atropine, kemadrine, and aturbán in controlling paralysis agitans while being less toxic and avoiding atropine-like side effects. Syntheses and pharmaceutical formulations are reported. E.g. di-Et 2-(2-pyridylmethyl)-2-phenylmalonate [3310-07-4] was added to Na and thiourea [62-56-6] and worked up to give 5-(2-pyridylmethyl)-5-phenyl-2-

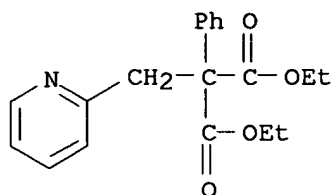
thiobarbituric acid [1454-06-4] which was oxidized using HNO₃ to 5-(2-pyridylmethyl)-5-phenylbarbituric acid [1454-05-3] which was reduced under acidic conditions to give I. Tablets each containing I 100, lactose 228, maize starch 70, Et cellulose 8, talc 20, and stearic acid 4 mg were prepared

IT **3310-07-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 3310-07-4 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)

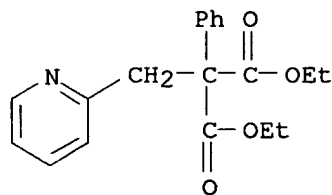


IT **1454-12-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 1454-12-2 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 43 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1976:90045 CAPLUS
DN 84:90045
TI Total synthesis of (+)-steganacin
AU Kende, Andrew S.; Liebeskind, Lanny S.
CS Dep. Chem., Univ. Rochester, Rochester, NY, USA
SO Journal of the American Chemical Society (1976), 98(1), 267-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 84:90045
GI For diagram(s), see printed CA Issue.
AB The total synthesis of the antileukemic dibenzocyclooctadiene lignan

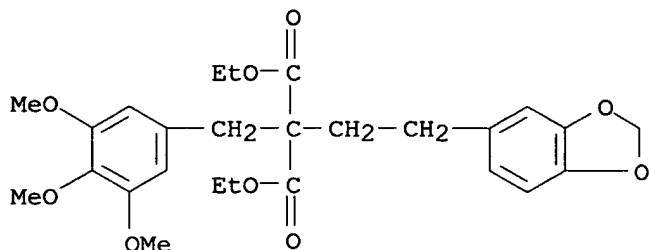
lactone steganacin (I, R = COMe) in the racemic form, along with companion lactones (\pm)-steganol (I, R = H) and (\pm)-steganone (II), was achieved starting from homopiperonyl alc. Formation of the 8-membered ring was carried out by VOF3 nonphenolic oxidative coupling, and C-5 O was regiospecifically introduced using N-bromosuccinimide, followed by silver trifluoroacetate. The yield from homopiperonyl alc. to (\pm)-steganone was 10% over 8 steps.

IT **58745-52-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 58745-52-1 CAPLUS

CN Propanedioic acid, [2-(1,3-benzodioxol-5-yl)ethyl][(3,4,5-trimethoxyphenyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 44 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1974:70639 CAPLUS

DN 80:70639

TI Indole derivatives. LXXXVII. Improvement in the synthesis of skatyl- and substituted skatylmalonic esters

AU Suvorov, N. N.; Velezheva, V. S.; Vampilova, V. V.

CS Mosk. Khim.- Tekhnol. Inst. im. Mendeleeva, Moscow, USSR

SO Khimiya Geterotsiklicheskikh Soedinenii (1973), (11), 1512-14

CODEN: KGSSAQ; ISSN: 0132-6244

DT Journal

LA Russian

GI For diagram(s), see printed CA Issue.

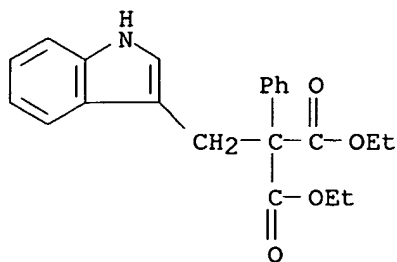
AB Gramine methiodide condensed with $\text{CHR}(\text{CO}_2\text{Et})_2$ Na salt (R = H, Et, Bu, Ph) in DMF at .apprx.100° in a N atmospheric to give the corresponding skatylmalonates I in 90-5% yield.

IT **51843-46-0P**

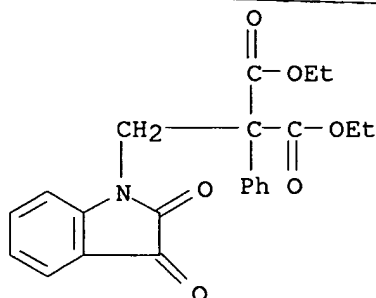
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 51843-46-0 CAPLUS

CN Propanedioic acid, (1H-indol-3-ylmethyl)phenyl-, diethyl ester (9CI) (CA INDEX NAME)

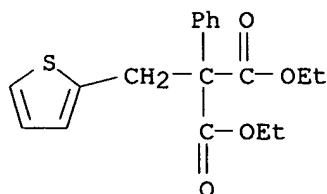


- L5 ANSWER 45 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1974:14805 CAPLUS
 DN 80:14805
 TI N-(α -Haloalkyl)carboxamides. 19. Reactions of N-(chloromethyl)isatin with prototropically active compounds
 AU Boehme, H.; Schwartz, H.
 CS Pharm.-Chem. Inst., Univ. Marburg, Marburg/L., Fed. Rep. Ger.
 SO Archiv der Pharmazie (Weinheim, Germany) (1973), 306(9), 684-92
 CODEN: ARPMAS; ISSN: 0365-6233
 DT Journal
 LA German
 GI For diagram(s), see printed CA Issue.
 AB Reaction of N-(chloromethyl)isatin (I) with $\text{RCH}(\text{CO}_2\text{Et})_2$ or Ph_2CHCHO gave the isatins II ($\text{R} = \text{Me}$ or Ph) and III, resp. Reaction of I with HNRR_1 gave the isatins IV ($\text{R} = \text{R}_1 = \text{Et}$, $\text{NRR}_1 = \text{piperidino}$ or morpholino). Reaction of I with alkoxides, phenoxides, and carboxylates gave the ethers and esters V [$\text{R} = \text{Me}$, Et , CMe_3 , Pr , $\text{C}_6\text{H}_3(\text{NO}_2)_2$ -2,4, or COPh]. Reaction of I with thiols gave the sulfides VI [$\text{R} = \text{Me}$, Et , $\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_2\text{CO}_2\text{H}$, $\text{CH}_2\text{CO}_2\text{Et}$, 2,5- $\text{Cl}_2\text{C}_6\text{H}_3$, or 2,4-(O_2N) $2\text{C}_6\text{H}_3$]. Reaction of I with alkali metal dithiocarbamates gave the dithiocarbamates VII ($\text{R} = \text{Me}$, Et , Ph , or CH_2Ph ; $\text{R}_1 = \text{H}$, Me , Et , or Ph ; $\text{NRR}_1 = 1\text{-pyrrolidinyl}$, piperidino , morpholino , or $\text{hexahydro-1-azepinyl}$).
 IT **50899-37-1P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 50899-37-1 CAPLUS
 CN Propanedioic acid, [(2,3-dihydro-2,3-dioxo-1H-indol-1-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)

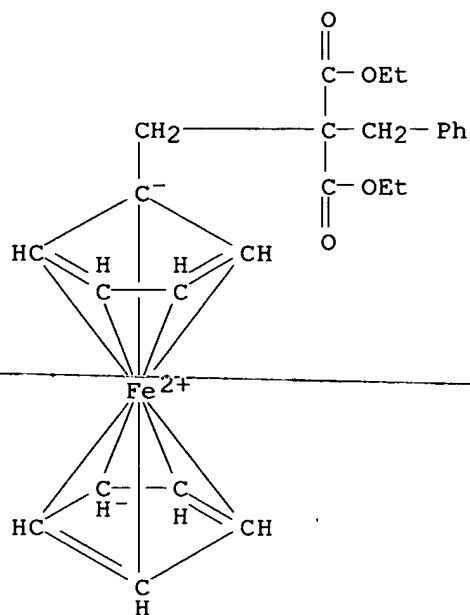


L5 ANSWER 46 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1974:3401 CAPLUS
 DN 80:3401
 TI Pharmaceutical (hexamethylenimino)alkyl compounds
 IN Robba, Max F.; Duval, Denise J. C.
 PA Innothera
 SO Ger. Offen., 38 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | DE 2313338 | A1 | 19731004 | DE 1973-2313338 | 19730317 <-- |
| | DE 2313338 | B2 | 19800626 | | |
| | DE 2313338 | C3 | 19810409 | | |
| | FR 2176473 | A1 | 19731102 | FR 1972-9639 | 19720320 <-- |
| | FR 2219776 | A1 | 19740927 | FR 1973-7505 | 19730302 <-- |
| | GB 1392671 | A | 19750430 | GB 1973-13910 | 19730322 <-- |
| | CA 1003831 | A1 | 19770118 | CA 1973-167040 | 19730326 <-- |
| | JP 48099190 | A2 | 19731215 | JP 1973-37370 | 19730330 <-- |
| | JP 51011117 | B4 | 19760408 | | |
| PRAI | FR 1972-9639 | A | 19720320 | | |
| | FR 1973-7505 | A | 19730302 | | |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | About 60 esters or amides (I, n = 2 or 3; X = O or NH; R = e.g. cyclohexyl, Ph, C ₆ H ₄ Cl-p, C ₆ H ₄ Br-p, CH ₂ Ph, R ₁ = R, C ₁ -5 alkyl, 2- or 3-thienyl, 2-thenyl, furfuryl, or 2-benzothienyl), β-(hexamethylenimino)ethyl (+)-cyclohexyl(3-thienyl)acetate, and their hydrochlorides, citrates, or oxalates were prepared and used as analgesics, vasodilators, local anesthetics, and spasmolytics. Thus, 4-BrC ₆ H ₄ CH(C ₆ H ₄ Cl-4)CO ₂ H and β-(hexamethylenimino)ethyl chloride was refluxed in Me ₂ -CHOH for 17 hr to give, after treatment with (CO ₂ H) ₂ , 70% I oxalate (n = 2, X = O, R = C ₆ H ₄ Br-4, R ₁ = C ₆ H ₄ Cl-4). DL-Et cyclohexyl(3-thienyl)acetate and β-(hexamethylenimino)ethanol was heated in PhMe in the presence of Na to give 70% DL-I (n = 2, X = O, R = cyclohexyl, R ₁ = 3-thienyl), which was resolved into the D and L form via the quinine salts. Ph ₂ CH-COCl and [2-(hexamethylenimino)ethyl]amine was refluxed in C ₆ H ₆ to give 50% I.HCl (n = 2, X = NH, R = R ₁ = Ph). | | | | |
| IT | 51535-44-5P | | | | |
| | RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of) | | | | |
| RN | 51535-44-5 CAPLUS | | | | |
| CN | Propanedioic acid, phenyl(2-thienylmethyl)-, diethyl ester (9CI) (CA INDEX NAME) | | | | |



AN 1972:59727 CAPLUS
 DN 76:59727
 TI Metallocenes. XVIII. Stereochemistry of heterobridged and homobridged ferrocene ketones and alcohols
 AU Gautheron, Bernard; Leblanc, Jean C.
 CS Fac. Sci. Fondam. Appl., Univ. Dijon, Dijon, Fr.
 SO Bulletin de la Societe Chimique de France (1971), (10), 3629-36
 CODEN: BSCFAS; ISSN: 0037-8968
 DT Journal
 LA French
 GI For diagram(s), see printed CA Issue.
 AB Dimethylaminomethylferrocene methyl iodide in HCONMe₂ was condensed with RCH(CO₂Et)₂ in the presence of Na in PhMe; hydrolysis and decarboxylation of the products gave substituted ferrocenylpropionic acids. Cyclization of the acids with (CF₃CO)₂O, polyphosphoric acid, or by intramol. Friedel-Crafts reactions gave essentially heteroannular bridged ketones (I) and small amts. of homoannular bridged ketones (II, R=Me₂CH, PhCH₂, Bu, Et). I and II were isolated in racemic and active series and their reduction was stereospecific. Anal. of I by NMR and CD for active compds. suggested a specific conformation which agreed with the observed asym. induction and the "kinetic resolution" of the optically active carbinols (III).
 IT **36655-55-7P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 36655-55-7 CAPLUS
 CN Ferrocene, 1-[2,2-bis(ethoxycarbonyl)-3-phenylpropyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 48 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1972:59436 CAPLUS
 DN 76:59436

TI Spasmolytic-vasodilating β -(3-benzo[b]thienyl)propionic acid derivatives

IN Robba, Max F.; Duval, Denise J. C.

PA Innothera

SO Ger. Offen., 39 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | DE 2128887 | A | 19711216 | DE 1971-2128887 | 19710611 <-- |
| | DE 2128887 | B2 | 19730913 | | |
| | DE 2128887 | C3 | 19740418 | | |
| | FR 2092731 | A5 | 19720128 | FR 1970-21679 | 19700612 <-- |
| | FR 2092731 | B1 | 19730810 | | |
| | US 3865842 | A | 19750211 | US 1971-150747 | 19710607 <-- |
| | GB 1318473 | A | 19730531 | GB 1971-27563 | 19710611 <-- |
| | JP 50028434 | B4 | 19750916 | JP 1971-42068 | 19710612 <-- |
| | US 3954780 | A | 19760504 | US 1974-489545 | 19740718 <-- |
| | US 4035371 | A | 19770712 | US 1976-651223 | 19760122 <-- |
| PRAI | FR 1970-21679 | A | 19700612 | | |
| | US 1971-150747 | A3 | 19710607 | | |
| | US 1974-489545 | A3 | 19740718 | | |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I; R=e.g. CH₂CH:CH₂, PhCH₂, or 2-thenyl; R₁=e.g. H, CH₂CH₂NEt₂, β -pyrrolidinoethyl, β -morpholinoethyl, or 1-piperidino-2-propyl) of LD₅₀ .apprx.100-320 mg/kg i.p. in mice, the spasmolytic, vasodilating, antiserotonin, and local anesthetic activities of which were tested in rats and guinea pigs, were prepared by condensation of 3-(chloromethyl)benzo[b]thiophene (II) with RCH(CO₂Et)₂ in the presence of NaOEt, hydrolysis, saponification, decarboxylation via the free acids followed

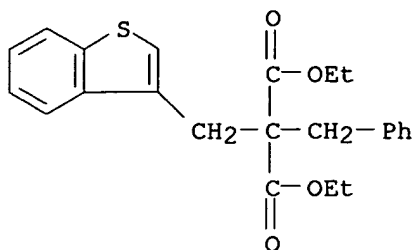
by aminoalkylation. Thus, CH₂:CHCH₂CH(CO₂Et)₂ was refluxed 1 hr with Na in EtOH, II in EtOH added, and the mixture refluxed 17 hr to give 70% Et allyl(benzo[b]thien-3-ylmethyl)malonate, which on 15 hr reflux with KOH-PhCH₂OH gave 80% I (R=CH₂:CHCH₂, R₁=H). Five other malonates and corresponding I (R₁=H) were similarly prepared I (R=Ph, R₁=H) and ClCH₂CH₂NEt₂ in iso-PrOH was refluxed 17 hr to give I (R=Ph, R₁=CH₂CH₂NEt₂), which was isolated as crystalline oxalate in 65% yield. Similarly prepared were 55 other I salts.

IT 35062-44-3P 35062-45-4P

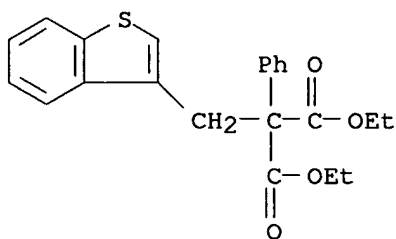
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 35062-44-3 CAPLUS

CN Propanedioic acid, (benzo[b]thien-3-ylmethyl)(phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 35062-45-4 CAPLUS

CN Propanedioic acid, (benzo[b]thien-3-ylmethyl)phenyl-, diethyl ester (9CI)
(CA INDEX NAME)

L5 ANSWER 49 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1971:12977 CAPLUS

DN 74:12977

TI Synthesis of quinolizine derivatives. XXIII. Synthesis of
perhydrobenzo[c]quinolizine and benzo[c]quinolizidine derivatives

AU Akiba, Mitsuo; Ohki, Sadao

CS Tokyo Coll. Pharm., Tokyo, Japan

SO Yakugaku Zasshi (1970), 90(10), 1193-200

CODEN: YKKZAJ; ISSN: 0031-6903

DT Journal

LA Japanese

GI For diagram(s), see printed CA Issue.

AB Perhydrobenzo[c]quinolizine derivs. I and II and a benzo[c]quinolizidine
derivative (III) were synthesized from quinaldine involving di-Et
β-(2-quinoyl)ethylmalonate intermediates.~~IT 30015-42-0P~~~~RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)~~

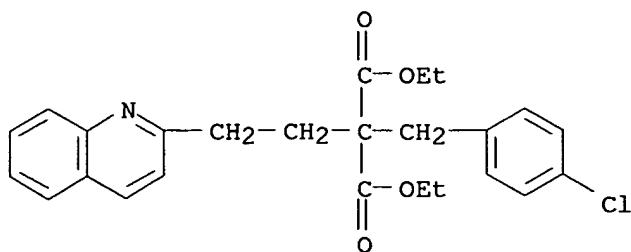
RN 30015-42-0 CAPLUS

CN Malonic acid, (p-chlorobenzyl)[2-(2-quinolyl)ethyl]-, diethyl ester,
monopicrate (8CI) (CA INDEX NAME)

CM 1

CRN 47674-45-3

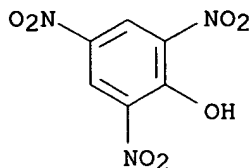
CMF C25 H26 Cl N O4



CM 2

CRN 88-89-1

CMF C6 H3 N3 O7



L5 ANSWER 50 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1970:520733 CAPLUS

DN 73:120733

TI Metallocenes. XV. Application of a specific reaction of ferrocenylcarbinols to the synthesis of mono and 1,2-disubstituted ferrocenes. Study of several stereochemical problems

AU Moise, Claude; Tirouflet, Jean

CS Lab. Chim. Org. Gen., Fac. Sci., Dijon, Fr.

SO Bulletin de la Societe Chimique de France (1970), (7), 2656-65

CODEN: BSCFAS; ISSN: 0037-8968

DT Journal

LA French

GI For diagram(s), see printed CA Issue.

AB 1,2-HOCH₂FcCH₂N+Me₃ I- (I, FcH₂ = ferrocene) reacted with refluxing alc. NaCr(CO₂Et)₂ (II, R = H, Me, Ph) to give the corresponding 1,2-Fc[CH₂Cr(CO₂Et)₂]₂, which gave 1,2-Fc(CH₂CHRCO₂H)₂ (III) after

saponification

and heating to 180° with powdered Cu. Treatment of III (R = H) with (CF₃CO)₂O in CH₂Cl₂ afforded IV, which was reduced to V by Zn(Hg) and HCl. Reaction of V with (CF₃CO)₂O in CH₂Cl₂ gave a mixture of VI and VII. KBH₄ reduction of VI gave a racemic mixture of alcs. LiAlH₄ reduction of VII gave

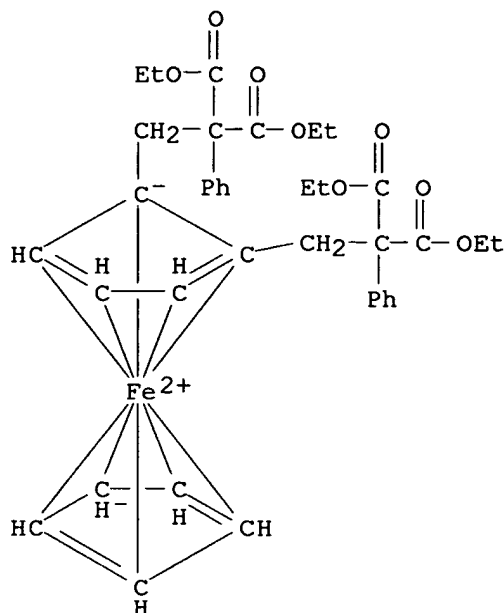
only

the endo-alc., which was converted to the exo isomer by refluxing the endo-acetate in aqueous Me₂CO 40 hr. The Et ester of IV was reduced to VIII by NaBH₄. HFcCH₂OH likewise reacted with II, and HFcCR₁R₂OH (R₁, R₂ = H, Me, Ph) reacted with II (R = H) to form HFcCR₁R₂CH(CO₂Et)₂; the latter was decarboxylated to give HFcCR₁R₂CH₂CO₂H (IX). IX (R₁, R₂ = Me) was cyclized and reduced with KBH₄ as above. These reactions were possible due to the stability of HFcCR₁R₂⁺. The stereochemistry of the reactions is discussed.

IT 31852-27-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 31852-27-4 CAPLUS

CN Malonic acid, (1,2-ferrocenediylldimethylene)bis[phenyl-, tetraethyl ester
(8CI) (CA INDEX NAME)

L5 ANSWER 51 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1970:413946 CAPLUS

DN 73:13946

TI Aromatic fluoro derivatives. XL. Effect of a pentafluorophenyl ring on the strength of CH-acids

AU Vlasov, V. M.; Krivousova, E. D.; Yakobson, G. G.

CS Novosibirsk. Inst. Org. Khim., Novosibirsk, USSR

SO Zhurnal Organicheskoi Khimii (1970), 6(4), 758-67

CODEN: ZORKAE; ISSN: 0514-7492

DT Journal

LA Russian

AB The action of NaH on C₆F₅CH₂CN in MeOCH₂CH₂OMe (I) solution gives p-NCCH₂C₆F₄CH(CN)C₆F₅ (II) which at -10° to 25° forms with the excess NaH colored carbanion p-NCCH₂C₆F₄C⁻(Na⁺)(CN)C₆F₅ (III). The existence of III was established by ir and NMR spectroscopy. The hydrolysis of II gave the corresponding dicarboxylic acid. Similarly, C₆F₅CH(CO₂Et)₂ in I solution gave stable C₆F₅C⁻(Na⁺)(CO₂Et)₂ (IV). The comparison of IV NMR spectra in I and PO(NMe₂)₃ (highly polar solvent) with the spectra of RC⁻(Na⁺)(CO₂Et)₂ (V) [R is p-HC₆F₄, 2,4-(O₂N)₂C₆H₃, o-O₂NC₆H₄, p-O₂HC₆H₄, or Ph] shows that the ionization of IV is of the same order as that of V (R = o-O₂NC₆H₄ or p-O₂NC₆H₄). The position of equilibrium was established in RCH(CO₂Et)₂ + IV. ¹H NMR. V + C₆F₅CH(CO₂Et)₂ systems. The relative reactivity of IV and V toward N-chloromethylphthalimide was determined

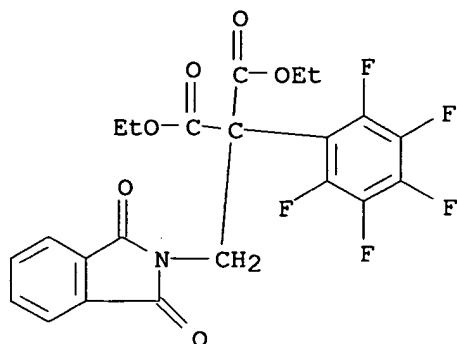
IT 28744-78-7P 28744-79-8P 28744-80-1P

28744-81-2P 28744-82-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

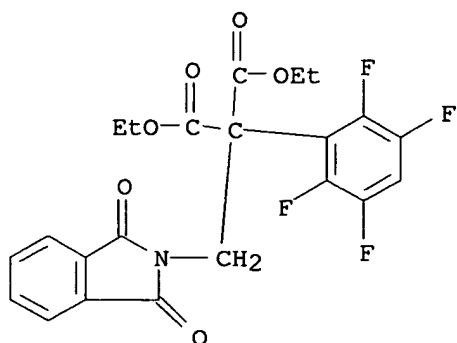
RN 28744-78-7 CAPLUS

CN Malonic acid, (pentafluorophenyl)(phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



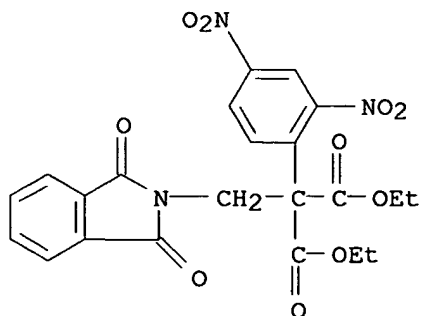
RN 28744-79-8 CAPLUS

CN Malonic acid, (phthalimidomethyl)(2,3,5,6-tetrafluorophenyl)-, diethyl ester (8CI) (CA INDEX NAME)

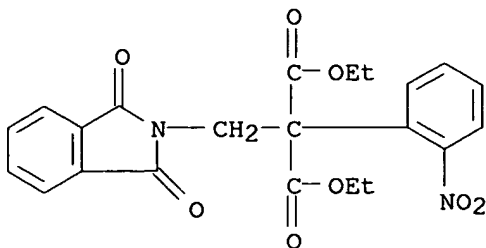


RN 28744-80-1 CAPLUS

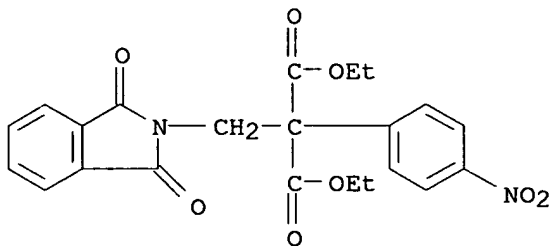
CN Malonic acid, (2,4-dinitrophenyl)(phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



RN 28744-81-2 CAPLUS

CN Malonic acid, (o-nitrophenyl) (phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)

RN 28744-82-3 CAPLUS

CN Malonic acid, (p-nitrophenyl) (phthalimidomethyl)-, diethyl ester (8CI)
(CA INDEX NAME)

L5 ANSWER 52 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1970:101087 CAPLUS

DN 72:101087

TI Analogs of angiotensin II. I. Solid phase synthesis

AU Chaturvedi, N. C.; Park, Won Kil; Smeby, R. R.; Bumpus, F. M.

CS Res. Div., Cleveland Clin. Found., Cleveland, OH, USA

SO Journal of Medicinal Chemistry (1970), 13(2), 177-81

CODEN: JMCMAR; ISSN: 0022-2623

DT ~~Journal~~

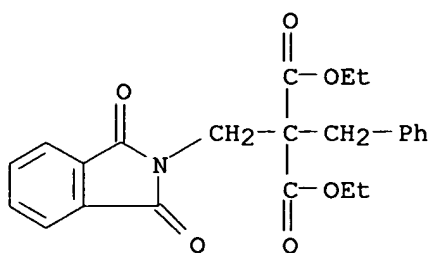
LA English

AB [5-Ile,8-Tyr]-, [5-Ile,8-(OMe)Tyr]-, [5-Val,8-(OMe)Tyr]-, [4-(OMe)-Tyr,5-Ile]-, [4-(OMe)Tyr,5-Val]-, [1-Asp(NH₂),4-(OMe)Tyr,5-Val]-, [5-Ile,7-pipecolic acid]-, [5-Ile,8-(3-amino-4-phenyl)-butyric acid]-, and [5-Ile,8-(3-amino-3'-phenyl)isobutyric acid]-angiotensins II were synthesized by the solid phase method in yields of 50-63%. All peptides were homogeneous. Insertion of OH or OMe on the Ph ring in position 8 of angiotensin II reduced pressor activity slightly. However, OMe in place of the OH of tyrosine in position 4 of angiotensin II caused a drastic reduction of pressor activity. Substitution of an unnatural amino acid in positions 7 or 8 of angiotensin II greatly reduced pressor activity.

IT **26217-38-9P**RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 26217-38-9 CAPLUS

CN Malonic acid, benzyl(phthalimidomethyl)-, diethyl ester (8CI) (CA INDEX NAME)



L5 ANSWER 53 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1970:31707 CAPLUS

DN 72:31707

TI 2,1,3-Thia- and selenadiazoles. LIX. Carboxy-, carboxymethyl-, and carboxyethylbenzo-2,1,3-thiadiazoles

AU Pesin, V. G.; D'yachenko, S. A.; Golubeva, E. V.

CS Leningrad. Khim.-Farm. Inst., Leningrad, USSR

SO Khimiya Geterotsiklicheskikh Soedinenii (1969), (4), 619-22

CODEN: KGSSAQ; ISSN: 0132-6244

DT Journal

LA Russian

GI For diagram(s), see printed CA Issue.

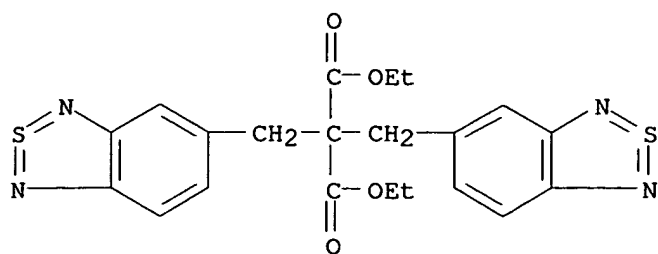
AB To a solution of 0.23 g Na in 15 ml anhydrous EtOH was added 1.6 g di-Et malonate, the mixture stirred 1 hr, and 2.29 g I (R = Br) in 25 ml dry C6H6 added, and the whole kept 10 hr to yield 81% I (R = CH2CO2H), m. 103-4° (H2O). To a solution of 0.92 g Na in 40 ml EtOH was added 6.4 g di-Et malonate, the mixture stirred 1 hr, and 9.2 g II (R = Br) in 80 ml dry EtOH added to yield 29% III (R = R1 = CO2Et) (IV), m. 105-6° (EtOH), and, from the mother liquor (after 8-10 hr reflux with 120 ml 20% HCl) 4.8 g II (R = CH2CO2H), m. 117-18° (H2O). IV (2 g) in 40 ml 10% KOH was refluxed 3 hr to give 90% III (R = H, R1 = CO2H), m. 141-2° (EtOH). To 10 ml HNO3 (d. 1.5) was added dropwise with stirring 1 g II (R = CO2H) and the mixture kept 30 min at 20° to give 73% V (R = CO2H), m. 180-2° (EtOH). To a solution of 1.5 g KCN in 75 ml EtOH and 5 ml H2O was added portionwise 2 g I (R = Br) and the whole refluxed 3 hr to yield 0.6 g VII (R = CN) (VIII), m. 192-3° (AcOH), and 1 g I (R = CN), m. 92-3° (EtOH). VIII (1 g) in 25 ml 50% H2SO4 and 25 ml AcOH was refluxed 3 hr to yield 95% VII (R = CO2H), m. 179-80° (EtOH). To 12 ml HNO3 (d 1.5) was added portionwise at 0° during 30 min 1 g II (R = CH2CO2H), and the mixture stirred 30 min and poured on ice to yield 85% V (R = CH2CO2H), m. 153-4° (aqueous EtOH). To 15 ml HNO3 (d. 1.5) was added portionwise at 0° with stirring 1.5 g. I (R = CH2CO2H) to yield 75% VI (R = CH2CO2H), m. 137-8° (EtOH). The pK values of the acids obtained were measured and compared with those of the corresponding aromatic carboxylic acids.

IT 24786-03-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 24786-03-6 CAPLUS

CN Malonic acid, bis(2,1,3-benzothiadiazol-5-ylmethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



L5 ANSWER 54 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1970:21590 CAPLUS

DN 72:21590

TI β -(1-Naphthyl)propionic acid derivatives

AU Mndzhoyan, A. L.; Badalyan, V. E.

CS Inst. Tonkoi Org. Khim., Erevan, USSR

SO Armyanskii Khimicheskii Zhurnal (1969), 22(8), 671-87

CODEN: AYKZAN; ISSN: 0515-9628

DT Journal

LA Russian

GI For diagram(s), see printed CA Issue.

AB For the investigation of spasmolytic properties a series of amino esters of α -substituted β -(1-naphthyl)propionic acids were synthesized. By known methods were prepared the following substituted furfuryl alcs. (Ia) (R1, R2, % yield, and b.p./mm. given): H, p-MeOC6H4CH2, 84.5, 187-8°/5; H, 3,4-(MeO)2C6H3CH2, 52.7, 210-12°/5; Me, Me, 89.9, 95-6°/10; PhCH2, Me, 74.2, 167-9°/5. Mono-substituted malonic acid esters were prepared in the usual way based on chlorides. The following RCH2CH(CO2Et)2 were obtained (R, % yield, and b.p./mm. given): 2-benzofuryl (A), 67.8, 179-82°/3; 5-methyl-2-furyl (B), 37.7, 132-5°/3; 5-benzyl-2-furyl (C), 55.6, 201-3°/3; 5-(p-methoxybenzyl)-2-furyl (D), 54.7, 222-4°/1; 5-(3,4-dimethoxybenzyl)-furyl (E), 44.1, 236-8°/1; 4,5-dimethyl-2-furyl (F), 30.8, 152-4°/3; 5-methyl-4-benzyl-2-furyl (G), 58.9, 204-6°; The introduction of the second radical, α -methylnaphthyl, was described. To 0.2 mole NaOEt in 150 ml EtOH was added 0.2 mole of the resp. monosubstituted malonate, the mixture refluxed 3 hr, cooled, and treated with 0.21 mole α -(chloromethyl)naphthalene, refluxed 12 hr., poured into H2O and extracted with Et2O. The following C10H7CH2C(RCH2)(CO2Et)2 were prepared (R, % yield, and b.p./mm. given): A, 83, 254-6°/1; B, 77.5, 222-5°/1; C, 74.6, 282-4°/1; D, 74.8, 302-3°/0.8; E, 64.9, 307-9°/0.6; F, 55.3, 233-5°/1; G, 63.5, 297-9°/1; By sap on. and decarboxylation, the following C10H7CH2CH(RCH2)CO2H were prepared (R, % yield, b.p./mm., and m.p. given): tetrahydrofuryl (H), 82.6, 225-6°/3, -; furyl (J), 79.3, 218-20°/3, 72-4°; A, 71.5, 259-61°, 111-12°; B, 73.0, 228-30°/3, 68-70°; C, 75.2, 280-3°/1, 70-2°; D, 82.5, 274-6°/0.4, -; E, 74.2, 285-8°/0.4, 61-2°; F, 55.4, 230-2°, -; G, 70.5, 264-6°/0.4, 51-2°. The substituted acid chlorides were prepared by refluxing 0.1 mole acid in 150 ml C6H6 with 0.13 mole SOCl2 4 hr, removing the solvent and distillation in vacuo. The following α -C10H7CH2CH(CH2R)COCl were obtained (R, % yield, and b.p./mm given): H, 74.2, 201-2°/1; J, 78.2, 190-2°/1; A, 80.6, 228-30°/1; B, 70.5,

202-4°/1; C, 87.3, 277-80°/1; D, 75.0, 280-2°/0.6; E, 69.4, 285-6°/0.4; F, 72.6, 210-2°/1; G, 74.1, 253-5°/0.6.

Amino esters were prepared by refluxing 0.1 mole of the acid chloride in 100 ml C₆H₆ and 0.12 mole 1,2-dimethyl-3-(dimethylamino)-propanol in 30 ml C₆H₆ 4 hr. The following amino esters α-C₁₀H₇CH₂CHRCO₂(CHMe)₂CH₂NMe₂ were prepared (R, % yield, and b.p./mm given):

H, 90.6, 182-3°/1; tetrahydrofurfuryl, 46.3, 233-5°/1; furfuryl, 84.7, 226-7°/1; benzofurfuryl, 88.3, 261-62°/1;

2-methyl-5-furfuryl (K), 82.5, 233-4°/1; 2-benzyl-5-furfuryl (L), 76.3, 280-2°/0.8; 2-(p-methoxybenzyl)furfuryl (M), 77.3, 304-5°/0.6; 2-(4,5-methoxybenzyl)-5-furfuryl (N), 74.1, 302-4°/0.6; 2,3-methyl-5-furfuryl (O), 70.8, 239-40°/1;

2-methyl-3-benzyl-5-furfuryl (P), 76.3, 248-50°/0.2. The diethylamino esters were obtained similarly using HNet₂ (R, % yield, and b.p./mm. given). H, 89.8, 188-90°/1; tetrahydrofurfuryl, 42.7, 240-1°/1; furfuryl, 81.3, 233-4°/1; benzofurfuryl, 85.1, 270-1°/1; K, 83.1, 240-1°/1; L, 79.5, 287-8°; M, 78.8, 310-1°/0.6; N, 76.8, 308-10°/0.4; O, 72.7, 240-2°/0.8. P, 68.3, 255-6°/0.2. Some derivs. of furfuryl alc. were prepared by reduction of substituted furyl-2-carboxylates with LiAlH₄.

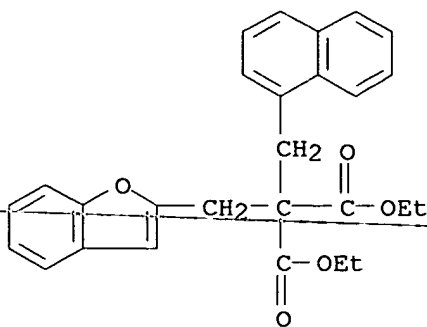
Di-Et 5-Benzylfurfurylidenemalonate, b.p. 220-2°, m. 43-4°, was obtained in the same way as the ester of furfurylidenemalonate. Also 95.2% 5-benzylfurfurylidenemalononic acid, m. 167° (decomposition), was prepared by saponification of the ester.

IT 25379-07-1P 25379-08-2P 25379-09-3P
25379-10-6P 25379-11-7P 25379-24-2P
25379-25-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

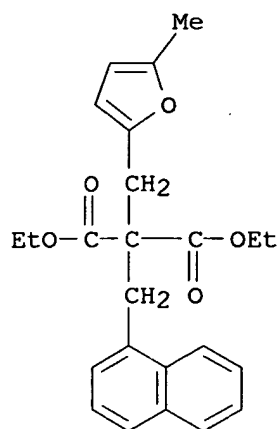
RN 25379-07-1 CAPLUS

CN Malonic acid, (2-benzofuranylmethyl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



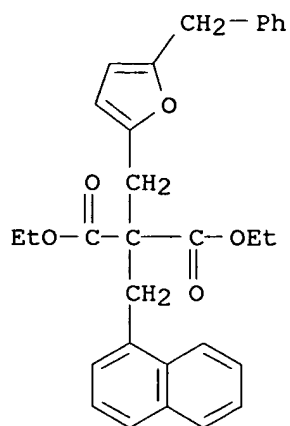
RN 25379-08-2 CAPLUS

CN Malonic acid, (5-methylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



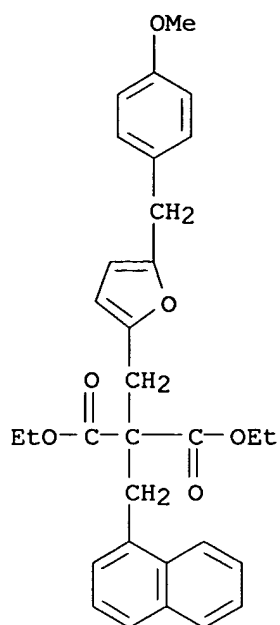
RN 25379-09-3 CAPLUS

CN Malonic acid, (5-benzylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI)
(CA INDEX NAME)



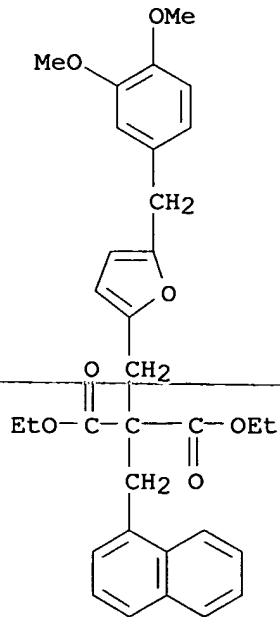
RN 25379-10-6 CAPLUS

CN Malonic acid, [5-(p-methoxybenzyl)furfuryl](1-naphthylmethyl)-, diethyl
ester (8CI) (CA INDEX NAME)



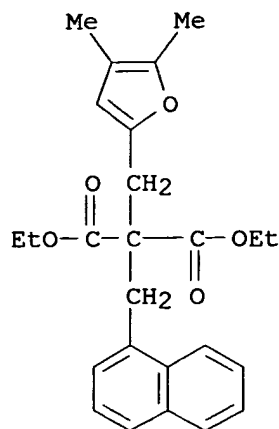
RN 25379-11-7 CAPLUS

CN Malonic acid, (1-naphthylmethyl)(5-veratrylfurfuryl)-, diethyl ester (8CI)
(CA INDEX NAME)



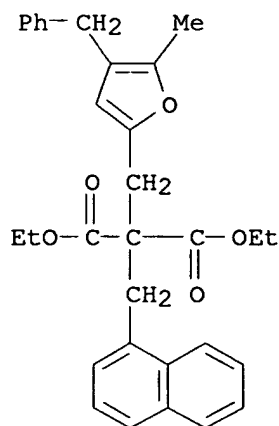
RN 25379-24-2 CAPLUS

CN Malonic acid, (4,5-dimethylfurfuryl)(1-naphthylmethyl)-, diethyl ester
(8CI) (CA INDEX NAME)



RN 25379-25-3 CAPLUS

CN Malonic acid, (4-benzyl-5-methylfurfuryl)(1-naphthylmethyl)-, diethyl ester (8CI) (CA INDEX NAME)



L5 ANSWER 55 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1969:524108 CAPLUS

DN 71:124108

TI ~~2-Phenylindol-3-yl methylation of methylene-active compounds~~

AU Buchmann, Gerhard; Voeltzke, W.

CS Tech. Hochsch. Chem. "Carl Schorlemmer", Leuna/Merseburg, Fed. Rep. Ger.

SO Pharmazie (1969), 24(8), 446-50

CODEN: PHARAT; ISSN: 0031-7144

DT Journal

LA German

GI For diagram(s), see printed CA Issue.

AB H₂C(CO₂Et)₂ (6.4 g.) was treated with 0.8 g. Na in PhMe, 11.5 g. 3-(trimethylammoniomethyl)-2-phenylindole methylsulfate added, and the mixture kept 2 hrs. at room temperature, 8 hrs. at 100°, and 110° until the reaction was complete, to give 57.5% I (R = H), m. 85°. The following I were similarly prepared (R, % yield, and m.p. given): Me, 15, 152°; Et, 36, 147°; Pr, 61, 162°; PhCH₂, 55,

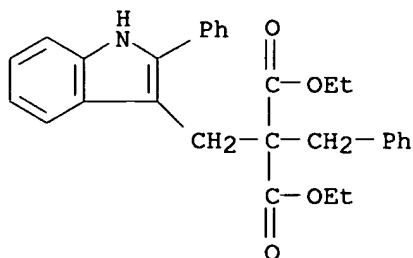
131°. Similarly prepared were the following II (R, R1, % yield, and m.p. given): H, CN, 81.7, 131°; Et, Ac, 49, 174°. Treatment of I (R = H) with NaOEt gave 53% 2-phenylindole together with EtO(CH₂)₂CO₂Et.

IT **23999-48-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23999-48-6 CAPLUS

CN Malonic acid, benzyl[(2-phenylindol-3-yl)methyl]-, diethyl ester (8CI)
(CA INDEX NAME)



L5 ANSWER 56 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1968:78157 CAPLUS

DN 68:78157

TI Quinolizidine derivatives

IN Matsuo, Ichiro; Ohki, Sadao

PA Chugai Pharmaceutical Co., Ltd.

SO Jpn. Tokkyo Koho, 2 pp.

CODEN: JAXXAD

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|-------------|------|----------|-----------------|--------------|
| PI | JP 42008626 | B4 | 19670418 | JP | 19640917 <-- |

GI For diagram(s), see printed CA Issue.

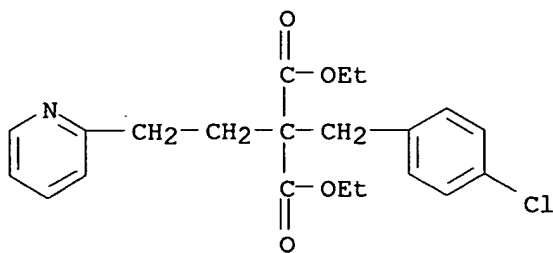
AB Na (2.2 g.) is added to a solution of 26 g. diethyl 2-(2-pyridyl)ethylmalonate in 200 ml. PhMe, the mixture heated at 110-15° for 10 hrs., 0.2 g. KI added, 17 g. p-chlorobenzyl chloride (I) added, the mixture heated 10 hrs. more, cooled, and filtered, the filtrate concentrated in vacuo and distilled in vacuo to remove unreacted I, the residue passed through a column of Al₂O₃ using C₆H₆-Me₂CO-(10:1), and the resulting solution evaporated to give 27.2 g. diethyl α-(p-chlorobenzyl) 2-(2-pyridyl)ethylmalonate (II), sirup. A solution of 19.5 g. II in 100 ml. AcOH is subjected to catalytic reduction using 1 g. PtO₂, the mixture filtered, the filtrate concentrated, the residue dissolved in H₂O, K₂CO₃ paste added and extracted with C₆H₆, the C₆H₆ extract concentrated, and the residue heated at 150-80° and distilled in vacuo to give 14 g. 3-carboethoxy-3-(p-chlorobenzyl)-4-oxoquinolizidine (III), b_{0.2} 185-95°, useful as an intermediate for the manufacture of 3-(p-chlorobenzyl)quinolizidine, useful as a uterus-contracting agent.

IT **17394-89-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 17394-89-7 CAPLUS

CN Malonic acid, (p-chlorobenzyl)[2-(2-pyridyl)ethyl]-, diethyl ester (8CI)
(CA INDEX NAME)



L5 ANSWER 57 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1967:37950 CAPLUS

DN 66:37950

TI Indolizine derivatives

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO U.S., 6 pp. Division of U.S. 3245990

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

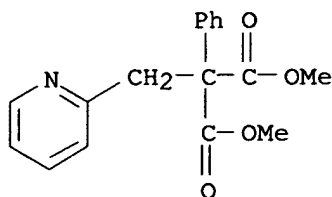
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| PI | US 3268535 | | 19660823 | US | 19650614 <-- |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | Division of U.S. 3,245,990 (CA 64, 19563e). Title compds. where R is H or Ph and R1 is Ph or hydroxyalkyl were prepared by treating an indolizinecarboxylic acid ester or the acid chloride with substituted piperazines. Thus, a mixture of 5 parts Na octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate, 2.6 parts oxallyl chloride, and 5 parts 1-phenylpiperazine was stirred at room temperature for 2 hrs., washed with dilute HCl, and dried to give octahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc). Other I prepared were (R, R1, and m.p. given): H, Ph, 162-4° (EtOAc); and Ph, HOCH2CH2, 179-80° (EtOAc). I are useful as anti-inflammatory and hypotensive agents. | | | | |

IT 3285-58-3P 3550-58-1P

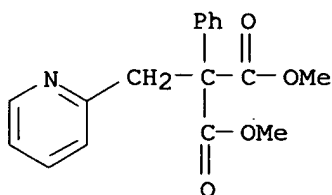
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 3285-58-3 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
(7CI, 8CI) (CA INDEX NAME)

● HCl

L5 ANSWER 58 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1967:2475 CAPLUS

DN 66:2475

TI Octahydro-3-oxoindolizines

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO U.S., 6 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|-----------------|--------------|
| PI | US 3274202 | | 19660920 | US | 19630402 <-- |

GI For diagram(s), see printed CA Issue.

AB Compds. of structure I were prepared Some of the products exhibited
~~hypotensive and central nervous system depressant activity.~~ A Knoevenagel
 condensation of 2-pyridinecarboxaldehyde 107 with $\text{CH}_2(\text{CO}_2\text{-Me})_2$ 145 in the
 presence of piperidine and BzOH yields dimethyl 2-pyridylmethylenemalonate
 (II) 180 parts, m. $83.5-4.5^\circ$ (aqueous MeOH). The diethyl analog (III)
 is similarly prepared (81%), b 0.5 157° ; sulfate m. $100-1.5^\circ$
 (EtOH-Et 2O). Treatment of II 125 with PhMgBr in C_6H_6 -Et 2O at $0-5^\circ$
 afforded dimethyl phenyl-2-pyridylmethylmalonate (IV) 81 parts as HCl
 salt, m. $175-8^\circ$ (decomposition) (EtOH-Et 2O); free base m. $97-8^\circ$
 (petr. ether-EtOAc). Reduction of III 10.8 over PtO 2 0.8 in absolute

EtOH-AcOH at

60 psi. gave ethyl octahydro-3-oxo-2-indolizine-carboxylate (V) 8.9 parts,
 b 0.06 $110-11^\circ$. The dimethyl analog (VI) was analogously prepared, b 1
 $138-45^\circ$. Similarly IV afforded methyl octahydro-3-oxo-1-phenyl-2-

indolizinecarboxylate (VII) as an isomer mixture, m. 84-9° (petr. ether-EtOAc); treatment of octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (m. 166-7°) with CH₂N₂ afforded the methyl ester, m. 113.5-14.0° (petr. ether-EtOAc). The ir spectrum is very similar, but not identical to VII. Condensation of VII 29.6 and PhCH₂Cl 25.3 with NaH in PhMe gave Me octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (VIII) 35.8 parts, b0.2 160°, and free acid 6.3 parts, m. 170° (decomposition). Saponification of VIII with NaOH in aqueous MeOH afforded the

free acid (as isomer mixture), m. 149-53° (EtOAc); repeated recrystn. yielded one isomer, m. 166-7°. Saponification of V gave 72% of the corresponding acid, m. 123-4.5° (Et₂O-CH₂Cl₂). Hydrolysis of VIII 23 with 10% NaOH (aqueous EtOH) gave octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid 16.9 parts, m. 177° (decomposition) (EtOAc). Reduction of VIII 10.6 with LiAlH₄ yielded octahydro-1-phenyl-2-indolizinemethanol (IX) 8.5 parts; fumarate m. 173-5° (decomposition) (iso-PrOH-Et₂O). Treatment of IX with MeI gave two methiodide fractions, one, an isomer mixture, m. 218.5-19.5° (EtOH); the other, a single isomer, m. 184-6°, with similar ir spectra. Octahydro-2-benzyl-2-indolizinemethanol-HCl (X), m. 235-7° (iso-PrOH), was similarly prepared from VIII. Octahydro-2-indolizinemethyl benzilate, m. 104-6° (n-heptane), was obtained from the corresponding amino alcohol and ethyl benzilate by transesterification; similarly IX yielded octahydro-1-phenyl-2-indolizinemethyl benzilate, m. 108-9° (hexane). Refluxing Na octahydro-3-oxo-2-indolizinecarboxylate 7.2 with 9.2 β-dimethylaminoethyl chloride in C₆H₆ 24 hrs. yielded 2-dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate 7.3 parts, b0.35 155°; fumarate m. 130-115° (sic) (EtOH-Et₂O). Similarly prepared were: 2-dimethylaminoethyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 161-3° (iso-PrOH-Et₂O); (1-methyl-4-piperidyl) octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 174-6° (EtOH-Et₂O); octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 162-4° (EtOAc); octahydro-3-oxo-2-[N-(2-dimethylaminoethyl)carbamoyl]indolizine, b0.35 174° [HCl salt m. 174-6° (iso-PrOH-Et₂O)]; octahydro-3-oxo-2-[N-(α-methylphenethyl)carbamoyl]indolizine, b0.075 185-92°. Preparing the acid chlorides from the corresponding Na salts and (COCl)₂ followed by reaction with the appropriate amine afforded: octahydro-3-oxo-2-[N-(3-pyridylmethyl)carbamoyl]indolizine, m. 115-16.5° (EtOAc-Et₂O); octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl)indolizine, m. 169-70° (EtOAc); octahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc); octahydro-3-oxo-1-phenyl-2-morpholinocarbonylindolizine, m. 128-9° (EtOAc); octahydro-3-oxo-1-phenyl-2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl]indolizine, m. 178-80° (EtOAc). Octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine dihydrochloride, m. 245.5-7.0° (EtOH-Et₂O), was prepared by LiAlH₄ reduction of the corresponding oxo compound. Analogously prepared were: octahydro-1-phenyl-1-morpholinomethylindolizine dihydrochloride, m. 270-2° (decomposition); octahydro-2-benzylindolizine, b0.15 97-100°; hexamate m. 108-120° (Me₂CO-Et₂O). Octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (XI) 70.6, yields on 10 min. heating as a melt 49.5 octahydro-3-oxo-2-benzylindolizine, b0.175 138°. Heating XI 4.5 with polyphosphoric acid 66 3 hrs. at 100° affords 1',5',6',7',8',8a'-hexahydro-1-oxospiro [indan-2,2'-indolizine]-3'(2'H)-one (XII) 4 parts, m. 121-2° (C₆H₁₂). Reduction of XII with LiAlH₄ gave octahydro-1-hydroxyspiro [indan-2,2'-indolizine], m.

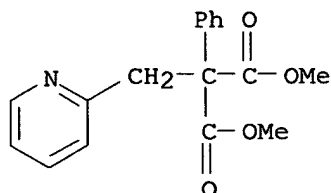
110-22° (C₆H₆-hexane). Reduction of XII 5.1 with NaBH₄ in iso-PrOH yielded 1',5',6',7',8',8a'-hexahydro-1-hydroxyspiro[indan-2,2'-indolizine]-3'(2'H)-one 3.3 parts, m. 137-42°, and m. 151-5° (C₆H₁₂); the mother liquor yielded an addnl. 0.2 part second isomer; a mixed m.p. with the isomeric mixture was depressed.

IT **3285-58-3P 3550-58-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

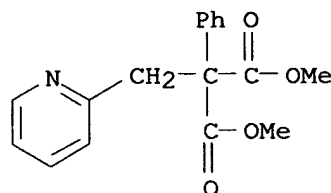
RN 3285-58-3 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 59 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1966:482196 CAPLUS

DN 65:82196

OREF 65:15351d-h,15352a-c

TI Octahydro-3-oxo-2-indolizinecarboxylic acids

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO 6 pp.

DT Patent

LA Unavailable

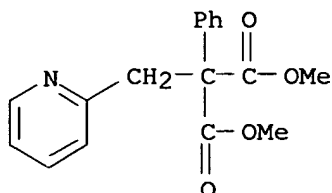
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| PI | US 3268540 | | 19660823 | US | 19650614 <-- |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | Compds. of the general formula I, where R1 is H or PhCH ₂ and R2 is CO ₂ H, CH ₂ OH, or a carbamoyl or a carboalkoxy group, are prepared and can be used | | | | |

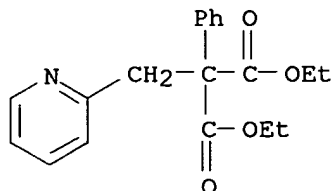
as hypotensive and antiinflammatory agents. Thus, a mixture of 107 parts 2-pyridinecarboxaldehyde, 145 parts $\text{CH}_2(\text{CO}_2\text{Me})_2$, 8 parts piperidine, 6.6 parts BzOH , and C_6H_6 is heated to give to give di-Me 2-pyridylmethylenemalonate (II), m. $83.5-4.5^\circ$ (aqueous MeOH). Similarly prepared is di-Et 2-pyridylmethylenemalonate sulfate (III sulfate), m. $100-1.5^\circ$ (EtOH-Et₂O). A solution of PhMgBr (196 parts PhBr and 30 parts Mg) in Et₂O is treated with a C_6H_6 solution of 125 parts II to give di-Me phenyl(2-pyridylmethyl)malonate, m. $97-8^\circ$ (ligroine-EtOAc); HCl salt m. $175-8^\circ$ (decomposition) (EtOH-Et₂O). Similarly prepared is di-Et phenyl(2-pyridylmethyl)malonate, m. $71.5-2^\circ$ (ligroine). III (10.8 parts) in a mixture of 100 parts EtOH and 4 parts HOAc is hydrogenated in the presence of 0.8 part Pt oxide to give 6.2 parts Et octahydro-3-oxo-2-indolinecarboxylate (IV), b0.06 $110-11^\circ$. Similarly prepared are the following I ($\text{R}_1 = \text{H}$; R, R_2 , and m.p. given): H, CO_2Me , -- (b1 $138-45^\circ$); Ph, CO_2Me , $84-9^\circ$ (ligroine-EtOAc). A solution of 29.6 parts I ($\text{R} = \text{R}_1 = \text{H}$, $\text{R}_2 = \text{CO}_2\text{Me}$) in 50 parts PhMe is treated with 8.3 parts 54.7% NaH in mineral oil to give 15% I ($\text{R} = \text{H}$, $\text{R}_1 = \text{PhCH}_2$, $\text{R}_2 = \text{CO}_2\text{H}$), m. 170° , and I ($\text{R} = \text{H}$, $\text{R}_1 = \text{PhCH}_2$, $\text{R}_2 = \text{CO}_2\text{Me}$), b0.2 160° . A mixture of 35 parts I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CO}_2\text{Me}$), 5 parts NaOH, and aqueous MeOH is refluxed to give I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CO}_2\text{H}$) (V), m. $166-7^\circ$ (EtOAc). I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CO}_2\text{Me}$) (10.6 parts) is treated with 6.9 parts LiAlH_4 to give I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_2\text{OH}$); fumarate m. $173-5^\circ$ (decomposition) (iso-PrOH-Et₂O); MeI salt, m. $218.5-19.5^\circ$. Similarly prepared is I ($\text{R} = \text{H}$, $\text{R}_1 = \text{PhCH}_2$, $\text{R}_2 = \text{CH}_2\text{OH}$) HCl salt, m. $235-7^\circ$ (iso-PrOH). A mixture of 0.2 part NaOMe, 6.8 parts I ($\text{R} = \text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_2\text{OH}$), 700 parts n-heptane, and 10.6 parts $\text{Ph}_2\text{C}(\text{OH})\text{CO}_2\text{Et}$ is refluxed to give 6.8 parts I [$\text{R} = \text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_2\text{O}_2\text{CC}(\text{OH})\text{Ph}_2$], m. $104-6^\circ$ (heptane). Similarly prepared is I [$\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_2\text{O}_2\text{CC}(\text{OH})\text{Ph}_2$], m. $108-9^\circ$ (hexane). V (6.8 parts) is treated with 1.05 parts NaOH to give I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CO}_2\text{Na}$). Also prepared are the following I ($\text{R}_1 = \text{H}$) (R, R_2 , and m.p. fumarate given): H, $\text{CO}_2\text{CH}_2\text{CH}_2\text{NMe}_2$, $113-15^\circ$; Ph, $\text{CO}_2\text{CH}_2\text{CH}_2\text{NMe}_2$, $161-3^\circ$; Ph, 1-methyl-4-piperidylcarbonyl, $174-6^\circ$; Ph, COCl , --. A mixture of 16.8 parts IV, a solution of 1.08 parts NaOMe in 165 parts MeOH, and 14.6 parts 4-phenylpiperazine is refluxed 28 hrs. to give 15.5 parts octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. $162-4^\circ$ (EtOAc). Also prepared are the following I ($\text{R}_1 = \text{H}$) (R, R_2 , and m.p. given): H, $\text{CONHCH}_2\text{CH}_2\text{NMe}_2$, -- (HCl salt m. $174-6^\circ$); H, $\text{CONHCHMeCH}_2\text{Ph}$, -- (b0.075 $185-92^\circ$); H, N-(3-pyridylmethyl)carbonyl, $115-16.5^\circ$; Ph, 1-pyrrolidinylcarbonyl, $169-70^\circ$; Ph, 4-phenylpiperazinocarbonyl, $164-5^\circ$; Ph, morpholinocarbonyl, $128-9^\circ$ (EtOAc); Ph, 4-(2-hydroxyethyl)piperazinocarbonyl, $179-80^\circ$ (EtOAc). I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{pyrrolidinylcarbonyl}$) is treated with 4.1 parts LiAlH_4 to give I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = 1\text{-pyrrolidinylmethyl}$)-2HCl m. $245.5-7^\circ$ (EtOH ether). Similarly prepared is I ($\text{R} = \text{Ph}$, $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{morpholinomethyl}$)-2HCl, m. $270-2^\circ$ (decomposition). I ($\text{R} = \text{H}$, $\text{R}_1 = \text{PhCH}_2$, $\text{R}_2 = \text{CO}_2\text{H}$) (VI) (70.6 parts) is heated to give 49.5 parts I ($\text{R} = \text{R}_2 = \text{H}$, $\text{R}_1 = \text{PhCH}_2$) (VII), b0.275 138° . VII (15 parts) is treated with 7.4 parts LiAlH_4 to give octahydro-2-benzylindolizine hexamate, m. $108-20^\circ$ (Me₂CO-Et₂O). A mixture of 4.5 parts VI and 66 parts polyphosphoric acid is heated 3 hrs. at 100° to give 2.8 parts 1',5',6',7',8',8a'-hexahydro-1-oxospiro(indan-2,2'-indolizin)3'(2'H)-one (VIII), m. $121-2^\circ$. VIII (7.7 parts) is treated with 3.4 parts LiAlH_4 to give 3 parts octahydro-1-hydroxyspiro(indan-2,2'-indolizine), m. $110-22^\circ$ (C_6H_6 -hexane). VIII (5.1 parts) in 50 parts iso-PrOH is added to 0.76 part NaBH_4 in 125 parts iso-PrOH and the mixture refluxed 2 hrs. to give 2.4 parts 1',5',6',7',8',8a'-hexahydro-1-hydroxyspiro(indan-2,2'-indolizin)-

3' (2'H)-one, m. 137-42° and 151-5°.

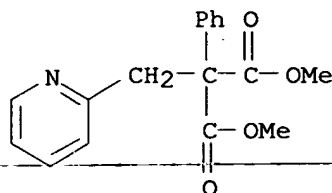
- IT 3285-58-3, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
 3310-07-4, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
 3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
 (preparation of)
 RN 3285-58-3 CAPLUS
 CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



- RN 3310-07-4 CAPLUS
 CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



- RN 3550-58-1 CAPLUS
 CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

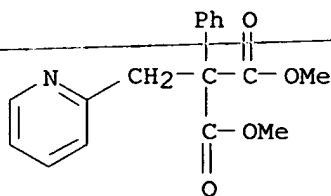
- L5 ANSWER 60 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1966:104086 CAPLUS
 DN 64:104086
 OREF 64:19563e-h
 TI 2-(Pyrrolidino and morpholino)carbonyl-3-oxooctahydroindolizines

IN Mohrbacher, Richard J.
 PA McNeil Laboratories, Inc.
 SO 6 pp.
 DT Patent
 LA Unavailable
 FAN.CNT 1

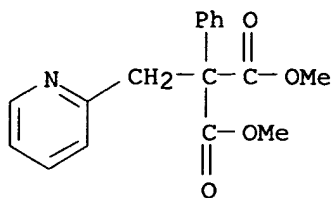
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | US 3245990 | | 19660412 | US | 19650614 <-- |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | Dimethyl 2-pyridylmethylenemalonate (22.1 g.) in 150 ml. EtOH and 10 ml. AcOH in the presence of PtO2 was hydrogenated under 4 atmospheric H to give | | | | |

14.3 g. methyl octahydro-3-oxo-2-indolizinecarboxylate (I, R = R1 = H, R2 = CO2Me), b1, 138-45°. A solution of 29.6 g. methyl octahydro-3-oxo-2-indolizinecarboxylate in 50 ml. PhMe was added during 15 min. to a suspension of 4.5 g. NaH in 250 ml. PhMe. Gas evolution stopped after refluxing 1 hr. A solution of 25.3 g. PhCH2Cl in 50 ml. PhMe was added to the stirred mixture at 100°. After 16 hrs. stirring at reflux the mixture gave 35.8 g. methyl octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (I, R = H, R1 = CO2Me, R2 = CH2Ph), b0.2 160°, and 6.3 g. octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (II), m. 170° (decomposition). During 20 min. 4.5 g. II was added to 66 g. polyphosphoric acid at 100°. After stirring 3 hrs. at 100° the mixture was worked up to give 4 g. III, m. 121-2° (cyclohexane). Also prepared were the following I (R, R1, R2, and m.p. or b.p.(mm.) given): H, CO2H, H, 123-4.5°; H, CO2H, CH2Ph, 177°; H, CO2Et, H, 110-11°(0.06); Ph, CO2H, H, 84-9°; H, CO2CH2CH2NMe2, H, 155°(0.35); Ph, 4-morpholinocarbonyl, H, 128-9°; Ph, 1-pyrrolidinylcarbonyl, H, 169-70°; H, CH2Ph, H, 138°(0.17). Also prepared was octahydro-2-benzyl-2-indolizinemethanol-HCl, m. 235-7°, and octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine-2HCl, m. 245.5-47°. The indolizines of this patent have various pharmacol. activities, including hypotensive, antiinflammatory, and central nervous system depressant.

IT 3285-58-3, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
 3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
 (preparation of)
 RN 3285-58-3 CAPLUS
 CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
 CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 61 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1966:93375 CAPLUS

DN 64:93375

OREF 64:17557b-h,17558a-c

TI Octahydroindolizines

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO 6 pp.

DT Patent

LA Unavailable

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|-----------------|--------------|
| PI | US 3245991 | | 19660412 | US | 19630402 <-- |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I), which possess hypotensive properties, antiinflammatory, and anticholinergic activity, were prepared, by the Knoevenagel condensation of 2-pyridinecarboxaldehyde (II) with a dialkyl malonate in the presence of a suitable condensing agent, and treating the resulting dialkyl 2-pyridylmethylenemalonate in a number of ways to produce the 1-Ph, and 2-PhCH₂ substituted derivs. A mixture of 107 II, 145 CH₂(CO₂Me)₂, 8 piperidine, and 6.6 parts BzOH was heated in C₆H₆ for 2.5 hrs. with azeotropic distillation of H₂O to give 180 parts dimethyl 2-pyridylmethylenemalonate (III), m. 83.5-4.58° (aqueous MeOH). Similarly prepcd. was diethyl 2-pyridinemethylenemalonate (IV), IV sulfate m. 100-1.5°. To an ethereal solution of PhMgBr (prepared from 196 PhBr and 30 parts Mg) was added dropwise during 1.5 hrs. at 0° to 5° a C₆H₆ solution of 125 parts III. The mixture was poured into cold dilute HCl and the aqueous layer worked up to give 81 parts dimethyl phenyl-2-pyridylmethylenemalonate (V), m. 97-8°, V.HCl m. 175-8°. IV similarly gave the corresponding diethyl phenyl-2-pyridylmethylenemalonate (VI), m. 71.5-2°. VI (10.8 parts) was reduced over 0.8 part Pt oxide in 100 parts EtOH and 4 parts AcOH at 60 psi. of H to give 6.2 parts Et octahydro-3-oxo-2-indolizinecarboxylate (VII), b_{0.06} 110-11°. III was similarly reduced to Me octahydro-3-oxo-2-indolizinecarboxylate (VIII), b₁ 138-45°. An ethanolic solution of 10 parts V containing 10 parts AcOH was hydrogenated at room temperature in the presence of 1 part Pt oxide at 51 psi. of H to give Me octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate (IX), m. 84-9° (IXa) and 113.5-14° (IXb). IXb was also obtained by treating octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (X), m. 166-7°, with CH₂N₂ in MeOH. A solution of 29.6 VIII in 50 PhMe was added dropwise during 15 min. to a suspension of NaH (8.3 parts 54.7% NaH in mineral oil) in 250 parts PhMe. The mixture was refluxed 1 hr. and

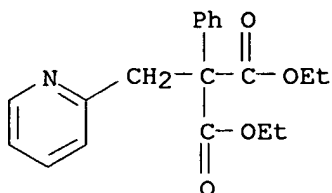
treated dropwise with stirring at 100° with 25.3 PhCH₂Cl in 50 parts PhMe. The mixture was stirred 16 hrs. at reflux, cooled, carefully treated with 5 parts absolute EtOH and 100 parts H₂O. The organic layer was worked up to give 6.3 parts octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (XI), m. 170° (with gas evolution), and 35.8 parts of the Me ester (XII) of XI, b_{0.2} 160°. An aqueous methanolic solution of 35 parts IX containing 5 parts NaOH was refluxed 3 hrs.

to

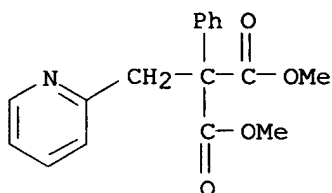
give a mixture of geometrical isomers of the free acid (X). Octahydro-3-oxo-2-indolizinecarboxylic acid (XIII), m. 123-4.5° was similarly obtained from its Et ester (VII). A mixture of 2.3 XII, 40 EtOH, and 50 parts 10% NaOH was refluxed 5 hrs. to give 16.9 parts XI. IX was reduced with 6.9 parts LiAlH₄ and the recovered product treated with 1.2 parts fumaric acid in MeOH to give I fumarate (R = Ph, R' = H, n = 1, R₂ = OH), m. 173-5° (decomposition). An ethereal solution of the above reduction product was treated with MeI for 50 hrs. to give the corresponding methiodide, m. 184-6° (one isomer), and m. 218.5-19.5° (mixture of isomers). XII was similarly reduced to I.HCl (R = H, R₁ = PhCH₂, n = 1, R₂ = OH), m. 235-7°. A suspension of 0.2 NaOMe, 6.8 I (R = R₁ = H, n = 1, R₂ = OH) (Ia), and 10.6 Et benzilate in 700 parts n-heptane was refluxed 1 hr. to give 6.8 parts I [R = R₁ = H, n = 1, R₂ = OCOC(OH)Ph₂], m. 104-6°. Similarly prepared was I (R = Ph, R₁ = H, n = 1, R₂ = OCOC(OH)Ph₂), m. 108-9°. A solution of 7.2 XIII and 1.6 NaOH in 50 parts H₂O-EtOH was evaporated and the dry residue, resuspended in 50 parts C₆H₆, was treated with a C₆H₆ solution of Me₂NCH₂CH₂Cl and refluxed 24 hrs. to give 2-dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate fumarate, m. 113-15°. Similarly prepared was 2-dimethylaminoethyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 161-3°. The acid chloride of X (prepared from 6.5 parts of the Na salt and 2.9 parts oxalyl chloride) was added dropwise to a solution of 3 parts 1-methyl-4-hydroxypiperidine in C₆H₆ and stirred 1 hr. at room temperature to give (1-methyl-4-piperidyl) octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate fumarate, m. 174-6°. The following were similarly prepared by the above procedures: octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl) indolizine, m. 162-4°; octahydro-3-oxo-2-[N-(2-dimethylaminoethyl) carbamoyl] indolizine, m. 174-6° (HCl salt); octahydro-3-oxo-2-[N-(α-methylphenethyl) carbamoyl] indolizine, b_{0.075} 185-92°; octahydro-3-oxo-2-[N-(3-pyridylmethyl) carbamoyl] indolizine, m. 115-16.5°; octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl) indolizine, m. 169-70°; octahydro-3-oxo-2-(4-phenyl-1-piperazinyl-carbonyl) indolizine, m. 164-5°; octahydro-3-oxo-2-morpholino-carbonyl indolizine, m. 128-9°; and octahydro-3-oxo-1-phenyl-2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl] indolizine, m. 179-80°. The following I derivs. were obtained by the procedures described above (R, R₁, n, R₂, and m.p. of the di-HCl salt given): Ph, H, 1, 1-pyrrolidinyl, 245.5-7°; and Ph, H, 1, morpholino, 270-2° (decomposition). XI (70.6 parts) was melted and heated 10 min. until no more gas evolved to give 49.5 parts octahydro-3-oxo-2-benzylindolizine (XIV), b_{0.175} 138°. XIV (15 parts) was reduced in the usual manner with LiAlH₄ and the recovered product converted to the hexamate salt of octahydro-2-benzylindolizine, m. 108-20°. XI (4.5 parts) was added portionwise during 20 min. to 66 parts polyphosphoric acid heated to 100°, and kept at 100° 3 hrs. with stirring to give 1',5',6',7',8',8'a-hexahydro-1-oxospiro(indan-2,2'-indolizin)-3'(2'H)-one (XV), m. 121-2°. XV was reduced with LiAlH₄, as above to give octahydro-1-hydroxyspiro(indan-2,2'-indolizine), m. 110-22°. XV (5.1 parts) in 50 parts iso-PrOH was added rapidly

to a suspension of 0.76 part NaBH₄ in 125 parts 2-PrOH and the mixture was refluxed 2 hrs. and worked up in the usual manner to give 2.4 parts 1',5',6',7',8',8'a-hexahydro-1-hydroxyspiro(indan-2,2'-indolizine)-3' (2'H)-one, m. 137-42° and m. 151-5°.

IT 3310-07-4, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
 3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
 (preparation of)
 RN 3310-07-4 CAPLUS
 CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS
 CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 62 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:462961 CAPLUS

DN ~~63:62961~~

OREF 63:11513b-h,11514a-d

TI Oxo- and hydroxyspiroindanindolizines

IN Mohrbacher, Richard J.

PA McNeil Laboratories, Inc.

SO 5 pp.

DT Patent

LA Unavailable

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | US 3189611 | | 19650615 | US | 19630402 <-- |
| GI | For diagram(s), see printed CA Issue. | | | | |
| AB | Compds. of the general structure, in which R1 is H or oxo and R2 is H, oxo, OH, or OCOR, have hypotensive, antiedema, and antiinflammatory | | | | |

activity. A mixture of 107 g. 2-pyridinecarboxaldehyde (I), 147 g. $\text{CH}_2(\text{CO}_2\text{Me})_2$, 8 g. piperidine, and 6.6 g. BzOH in C_6H_6 heated 2.5 hrs. with azeotropic distillation of H_2O , concentrated, diluted with Et_2O , washed with NaHCO_3 and H_2O , dried, evaporated, and triturated with aqueous MeOH gave 180 g. 2- $\text{C}_5\text{H}_4\text{NCH}:\text{C}(\text{CO}_2\text{Me})_2$ (II), m. $83.5-4.5^\circ$ (aqueous MeOH). I and $\text{CH}_2(\text{CO}_2\text{Et})_2$ similarly gave 81% 2- $\text{C}_5\text{H}_4\text{NCH}:\text{C}(\text{CO}_2\text{Et})_2$ (III), b0.5 157° ; sulfate m. $100-1.5^\circ$ ($\text{EtOH}-\text{Et}_2\text{O}$). Addition of 125 g. II in C_6H_6 to PhMgBr (from 30 g. Mg and 196 g. PhBr) at $0-5^\circ$ over 1.5 hrs., stirring 2 hrs. at 5° , pouring into dilute HCl , and partial neutralization of the aqueous layer with K_2CO_3 gave 81 g. 2- $\text{C}_5\text{H}_4\text{NCH}_2\text{CPh}(\text{CO}_2\text{Me})_2\cdot\text{HCl}$, m. $175-8^\circ$ (decomposition) ($\text{EtOH}-\text{Et}_2\text{O}$); free base (IV) m. $97-8^\circ$ (petroleum ether- EtOAc). III (51 g.) gave 35 g. 2- $\text{C}_5\text{H}_4\text{NCH}_2\text{CPh}(\text{CO}_2\text{Et})_2$ (V), m. $71.5-72^\circ$ (petroleum ether). Hydrogenation of 22.1 g. II on 1.25 g. PtO_2 in 150 ml. EtOH and 10 ml. HOAc gave 14.3 g. Me octahydro-3-oxo-2-indolizinecarboxylate (VI), b1 $138-45^\circ$. Hydrogenation of 10.8 g. III gave 8.9 g. Et octahydro-3-oxo-2-indolizinecarboxylate (VII), b0.06 $110-11^\circ$. Hydrogenation of 10 g. IV in EtOH and 10 ml. HOAc on 1 g. PtO_2 gave a mixture of isomers of Me octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate (VIII), m. $84-9^\circ$ (petroleum ether- EtOAc). Action on 29.6 g. VI in 50 ml. PhMe by 4.5 g. NaH in 250 ml. PhMe , followed by 25.3 g. PhCH_2Cl in 50 ml. PhMe 16 hrs. gave 6.3 g. octahydro-3-oxo-2-benzyl-2-indolizinecarboxylic acid (IX), m. 170° (gas evoln.) and 35.8 g. Me octahydro-3-oxo-2-benzyl-2-indolizinecarboxylate (X), b0.2 160° . Saponification of 35 g. VIII gave 29.3 g. mixed isomers of octahydro-3-oxo-1-phenyl-2-indolizinecarboxylic acid (XI) m. $149-53^\circ$ (EtOAc). Several recrystns. of X from EtOAc gave a single geometrical isomer, white prisms, m. 166.7° . Saponification of VII gave a 72% yield of mixed isomers of octahydro-3-oxo-2-indolizinecarboxylic acid (XII), m. $110-21^\circ$, from which a pure isomer, m. $123-4.5^\circ$ ($\text{Et}_2\text{O}-\text{CH}_2\text{Cl}_2$) was obtained. Saponification of 23 g. X by 50 ml. 10% NaOH and 40 ml. 95% EtOH and the mixture refluxed 5 hrs. gave 16.9 g. IX, m. 177° (gas evoln.) (EtOAc). Et octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate (13.2 g.) and 8.2 g. LiAlH_4 in Et_2O were refluxed 3.5 hrs., treated with 24.5 ml. H_2O , filtered, dried (MgSO_4), and concentrated to give 8.5 g. oil, octahydro-1-phenyl-2-indolizinemethanol (XIII).

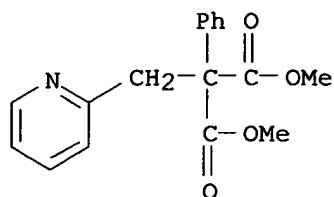
Treatment of this oil with 5 g. MeI 50 hrs. gave 7.3 g. solid, fractional crystallization of which from EtOH gave two isomers of octahydro-1-phenyl-2-indolizinemethanol methiodide, 4.1 g., m. $218.5-19.5^\circ$, and 0.8 g., m. $184-6^\circ$. Similar reduction of 10.6 g. VIII with 6.9 g. LiAlH_4 , followed by treatment of the oil with fumaric acid in MeOH , gave octahydro-1-phenyl-2-indolizinemethanol fumarate, m. $173-5^\circ$ (decomposition) (iso- $\text{PrOH}-\text{Et}_2\text{O}$). Reduction of 14.4 g. X by 5.7 g. LiAlH_4 and washing, drying, and concentration of the mixture, followed by HCl , gave octahydro-2-benzyl-2-indolizinemethanol hydrochloride, m. $235-7^\circ$ (iso- PrOH). A mixture of 6.8 g. octahydro-2-indolizinemethanol, 0.2 g. NaOMe , and 10.6 g. Et benzilate in 700 ml. C_7H_{16} was refluxed 1 hr., concentrated, diluted with Et_2O , and extracted with dilute HCl to give 6.8 g. octahydro-2-indolizinemethyl benzilate, m. $104-6^\circ$. Similar treatment of 9 g. XIII with 9.5 g. Et benzilate gave octahydro-1-phenyl-2-indolizinemethyl benzilate, m. $108-9^\circ$. The Na salt from 7.2 g. XII was refluxed 24 hrs. in C_6H_6 solution of $\text{Me}_2\text{NCH}_2\text{CH}_2\text{Cl}$ to give 7.3 g. β -dimethylaminoethyl octahydro-3-oxo-2-indolizinecarboxylate, b0.35 155° ; fumarate m. $113-15^\circ$ (iso- $\text{PrOH}-\text{Et}_2\text{O}$). Similarly obtained was β -dimethylaminoethyl octahydro-3-oxo-1-phenyl-1-indolizinecarboxylate, oil; fumarate m. $161-3^\circ$ (iso- $\text{PrOH}-\text{Et}_2\text{O}$). The acid chloride of XI (prepared from 6.5 g. XI Na salt and 2.9 g. $(\text{COCl})_2$)

and 3 g. 1-methyl-4-hydroxypiperidine in C₆H₆ gave 1-methyl-4-piperidyl octahydro-3-oxo-1-phenyl-2-indolizinecarboxylate, oil; fumarate m. 174-6° (EtOH-Et₂O). 4-Phenylpiperazine (14.6 g.) added to 16.8 g. VII and 1.08 g. NaOMe in 165 ml. MeOH, and the mixture refluxed 28 hrs. gave 15.5 g. octahydro-3-oxo-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 162-4° (EtOAc). Similarly, 16.8 g. VII and 14 g. Me₂NCH₂CH₂NH₂ gave 9.5 g. octahydro-3-oxo-2-[N-(2-dimethylaminoethyl)carbamoyl]indolizine, b_{0.35} 174°; hydrochloride m. 174-6° (iso-PrOH-Et₂O); and 19.7 g. VI and 15 g. (+)-amphetamine gave octahydro-3-oxo-2-[N-(α -methylphenethyl)carbamoyl]indolizine, b_{0.075} 185-92°. XI acid chloride (from 8.1 g. XI and 5.6 g. (COCl)₂) and 5.2 g. 3-aminomethylpyridine gave 5.5 g. octahydro-3-oxo-2-[N-(3-pyridylmethyl)carbamoyl]indolizine, m. 115-16.5° (EtOAc-Et₂O). Similarly prepared were octahydro-3-oxo-1-phenyl-2-(1-pyrrolidinylcarbonyl)indolizine (XIV), m. 169-70° (EtOAc); octahydro-3-oxo-1-phenyl-2-(4-phenyl-1-piperazinylcarbonyl)indolizine, m. 164-5° (EtOAc); octahydro-3-oxo-1-phenyl-2-morpholinocarbonylindolizine (XV), m. 128-9° (EtOAc); and octahydro-3-oxo-1-phenyl-2-[4-(2-hydroxymethyl)-1-piperazinylcarbonyl]indolizine, m. 179-80° (EtOAc). Action of 4.1 g. LiAlH₄ on 6.6 g. XIV in Et₂O 3 hrs., followed by 12 ml. H₂O, filtration, concentration, drying, and dry HCl treatment gave octahydro-1-phenyl-2-(1-pyrrolidinylmethyl)indolizine dihydrochloride, m. 245.5-47° (EtOH-Et₂O). Reduction of XV by LiAlH₄, followed by HCl, gave octahydro-1-phenyl-2-morpholinomethylindolizine dihydrochloride, m. 270-2° (decomposition). Thermal decarboxylation of 70.6 g. IX gave 49.5 g. octahydro-3-oxo-2-benzylindolizine, pale yellow-oil, b_{0.175} 138°, reduction of which by LiAlH₄ gave octahydro-2-benzylindolizine, b_{0.15} 97-100°; hexamate m. 108-20° (Me₂COEt₂O). A mixture of 4.5 g. IX and 66 g. polyphosphoric acid at 100° 3 hrs., poured onto crushed ice, and extracted with Et₂O/C₆H₆, gave 4 g. 1',5',6',7',8',8'- α -hexahydro-1-oxospiro(indan-2,2'-indolizine)-3'(2'H)-one (XVI), m. 121-2° (cyclohexane). LiAlH₄ (3.4 g.) and 7.7 g. XVI in 900 ml. Et₂O, refluxed 20 hrs., cooled, mixed with 10.4 ml. H₂O, filtered, extracted with 10% NaOH, washed, dried, and concd, gave 5.6 g. octahydro-1-hydroxyspiro(indan-2,1'-indolizine), m. 110-22° (C₆H₆-C₆H₁₄). Reduction of 5.1 g. XVI in 50 ml. iso-PrOH by 0.76 g. NaBH₄ in 125 ml. isoPrOH in 2 hrs. refluxing, followed by 125 ml. 2.9M HCl, concentration, extraction with Et₂O-C₆H₆, gave 3.8 g. oil; and an addnl. 0.6 g. oil was obtained by adding 35% NaOH to the aqueous layer, extracting with CH₂Cl₂, and concentrating Recrystn. of the oil, first from C₆H₆-C₆H₁₄, then from cyclohexane-C₆H₁₄ then from cyclohexane ultimately gave 0.2 g. of a single isomer of 1',5',6',7',8',8'- α -hexahydro-1-hydroxyspiro(indan-2,2'-indolizine)-3'(2'H)-one, m. 154-6°.

IT 3285-58-3, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester
 3310-07-4, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester
 3550-58-1, Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride
 (preparation of)

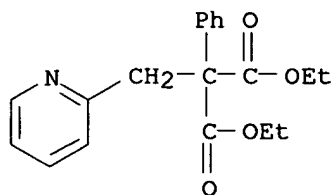
RN 3285-58-3 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester (7CI, 8CI) (CA INDEX NAME)



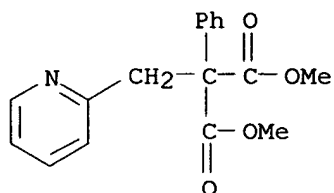
RN 3310-07-4 CAPLUS

CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 3550-58-1 CAPLUS

CN Malonic acid, phenyl(2-pyridylmethyl)-, dimethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L5 ANSWER 63 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:82624 CAPLUS

DN 62:82624

OREF 62:14694e-h,14695a-c

TI Barbituric acid derivatives

IN Wiggins, Leslie F.; James, John W.; Gittos, Maurice W.

PA Aspro-Nicholas Ltd.

SO 9 pp.; Division of Brit. 976,551

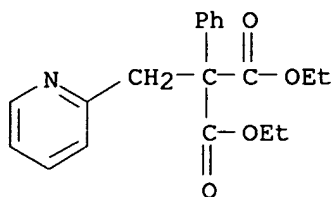
DT Patent

LA Unavailable

FAN.CNT 1

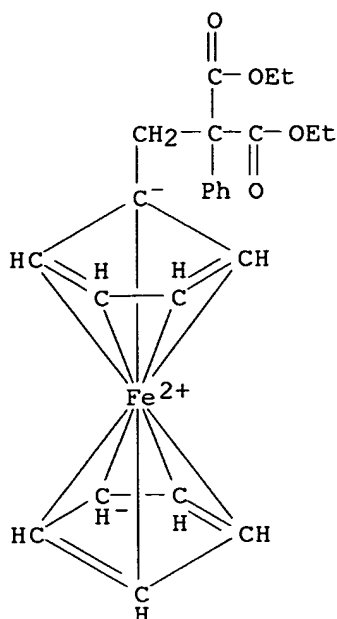
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------------------------------|------|----------|-----------------|--------------|
| PI | GB 977321 | | 19641209 | GB | 19591217 <-- |
| GI | For diagram(s), see printed CA Issue. | | | | |

- AB The title compds. (I) are prepared by condensation of a chloramine with a monosubstituted malonic ester to form a basic disubstituted malonic ester, $R_1R_2C(CO_2Et)_2$ (Ia) which is then condensed with urea or thiourea to give the I. Thus, a solution of 55 g. di-Et 2-phenylmalonate and 5.7 g. NaH in 150 ml. dry dioxane was stirred until effervescence ceased. The mixture was heated at 80° and 29 g. of 2-dimethylaminoethyl chloride added dropwise. After refluxing and stirring 3 hrs. the mixture was cooled, washed with ether and the aqueous layer acidified. Ether extraction of the acidic layer and distillation gave di-Et 2-(2-dimethylaminoethyl)-2-phenylmalonate (II), b0.001 118-24°. Treatment of II with Na in dry EtOH gave 5-(2-dimethylaminoethyl)-5-phenylbarbituric acid-HCl, m. 284-6°. Similarly prepared was di-Et 2-(2-pyridylmethyl)-2-phenylmalonate-HCl (III), m. 166-8°. Hydrogenation of III with PtO as catalyst gave di-Et 2-(2-piperidylmethyl)-2-phenylmalonate-HCl (IV), m. 174-5°. Treatment of IV with HCO_2H , HCO_2Na and 37-41% $HCHO$ in H_2O gave di-Et 2-(N-methyl-2-piperidylmethyl)-2-phenylmalonate (V), b0.15 140-7°. Treatment of V with thiourea and Na in anhydrous MeOH gave 5-(N-methyl-2-piperidylmethyl)-5-phenyl-2-thiobarbituric acid, m. 231-2°, (HCl salt m. 216-20°). Similarly prepared was 5-sec-amyl-5-(2-dimethylaminoethyl)-2-thiobarbituric acid-HCl, m. 265°. Treatment of 5-(2-diethylaminoethyl)-5-phenyl-2-thiobarbituric acid with 2.5N HNO_3 gave 5-(2-diethylaminoethyl)-5-phenylbarbituric acid, m. 193-4°. A MeOH solution of the free base of III was stirred with Na and thiourea in MeOH to give 5-(2-pyridylmethyl)-5-phenyl-2-thiobarbituric acid, m. 268°, which on treatment with 2.5N HNO_3 gave 5-(2-pyridylmethyl)-5-phenylbarbituric acid (VI), m. 320°. Hydrogenation of VI (PtO) gave 5-(2-piperidylmethyl)-5-phenylbarbituric acid-HCl, m. 197-9°, which refluxed with H_2O , HCO_2H , HCO_2Na , and 37-41% aqueous $HCHO$ gave 5-(N-methyl-2-piperidylmethyl)-5-phenylbarbituric acid-HCl hydrate, m. 195-200°. Treatment of 5-(2-dimethylaminoethyl)-5-(m-methoxyphenyl)-2-thiobarbituric acid in refluxing HOAc and concentrated HBr gave, after neutralization and treatment with HCl, 5-(2-dimethylaminoethyl)-5-(m-hydroxyphenyl)-2-thiobarbituric acid-HCl (VII), m. 270°. The oxo-analog, prepared as VI m. 269-71°. Similarly to II was prepared di-Et 2-(2-dimethylaminopropyl)-2-phenylmalonate, b0.1 116-20°, (H oxalate m. 144-6°). The malonates and barbiturates prep'd are given in the table. Treatment of thiourea dissolved in a solution of Na in anhydrous EtOH with di-Et 2-(2-diethylaminoethyl)-2-phenylmalonate gave 5-(2-diethylaminoethyl)-5-phenyl-2-thiobarbituric acid, m. 215° (HCl salt m. 234-6°). Similarly prepared was 5-(2-dimethylaminoethyl)-5-(o-chlorophenyl)-2-thiobarbituric acid, m. 236-8° (HCl salt m. 287-88°). These compds. are active in suppressing tremorine induced spasms in mice.
-
- IT 1454-12-2, Malonic acid, phenyl(2-pyridylmethyl)-, diethyl ester, hydrochloride
(preparation of)
- RN 1454-12-2 CAPLUS
- CN Propanedioic acid, phenyl(2-pyridinylmethyl)-, diethyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 64 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1964:440531 CAPLUS
 DN 61:40531
 OREF 61:7041d-g
 TI Heterobridged ketones derived from ferrocene
 AU Gautheron, Bernard; Triouflet, Jean
 CS Fac. Sci., Dijon, Fr.
 SO Compt. Rend. (1964), 258(26), 6443-5
 DT Journal
 LA Unavailable
 GI For diagram(s), see printed CA Issue.
 AB In this abstract Z = ferrocenyl radical (C₅H₅FeC₅H₄-). The sodio derivative of a substituted Et malonate, RCH(CO₂Et)₂, was prepared in xylene, powdered [ZCH₂NMe₃]⁺ I⁻ was added, and the product, ZCH₂CR(CO₂Et)₂, was isolated by chromatog. on Al₂O₃ [R = Me (I), m. 62°; R = Ph (II), m. 81°]. I was saponified to form ZCH₂CHMe(CO₂H)₂, decomposed 198°, which was decarboxylated to give ZCH₂CHMeCO₂H (III), m. 112°; II similarly gave directly ZCH₂CHPhCO₂H (IV), m. 98°. III or IV with (CF₃CO)₂O gave V (R = Me m. 102°; R = Ph m. 186°). The structures of the heterobridged ketones were established by mass, IR, and UV spectroscopy. The influence of the gem dialkyl group in promoting the latter reaction is attributed to steric effects. Polarog. measurements on the ketones did not show the expected inhibition of resonance of CO.
 IT 33111-48-7, Iron, cyclopentadienyl[(β,β-dicarboxyphenethyl)cyclopentadienyl]-, diethyl ester (preparation of)
 RN 33111-48-7 CAPLUS
 CN Ferrocene, [3-ethoxy-2-(ethoxycarbonyl)-3-oxo-2-phenylpropyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 65 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1964:404074 CAPLUS

DN 61:4074

OREF 61:608e-h,609a

TI α,α -Disubstituted diacids and their derivatives. XVII.

δ -Amino- α -phenylpentanoic acids

AU Salmon-Legagneur, F.; Neveu, C.

CS Ecole Natl. Super. Chim., Rennes

SO Bulletin de la Societe Chimique de France (1963), (10), 2175-89

CODEN: BSCFAS; ISSN: 0037-8968

DT Journal

LA Unavailable

OS CASREACT 61:4074

GI For diagram(s), see printed CA Issue.

AB cf. CA 59, 6300h. Benzyl cyanide derivatives (0.2 mole) were refluxed with 0.225 mole NaNH_2 in 300 ml. C_6H_6 , cooled, and refluxed 3-4 hrs. with 0.20 mole γ -bromopropylphthalimide in 20 ml. HCONMe_2 . After dilution with H_2O , Et_2O extraction, and evaporation, I was obtained (R, m.p., and % yield

given): H, 110° , 62; Ph, $173-4^\circ$, 75; PhCH_2 , 108° , 73; PhCH_2CH_2 , 109° , 72; Et, 83° , 59; Pr, $90-1^\circ$, 58; Bu, 80° , 55.5; cyclohexyl, 131° , 54. Similarly, II was prepared (same data): H, $89-90^\circ$, 77; Ph, 125° , 76; PhCH_2 , 98° , -; Et, 80° , 45; Pr, 117° , 45; Bu, 77° , 48; C_6H_{11} , $114-15^\circ$, -. I or II (0.1 mole) refluxed a week in 200 ml. 66% HBr and 100 ml. AcOH gave $\text{PhCR}(\text{CO}_2\text{H})\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2\cdot\text{HBr}$ (III) (same data): Ph, 260° , 90-95; PhCH_2 , 174° , 82; PhCH_2CH_2 , 214° , 72; Et, 161° , 74-95; Pr, 178° , 72-90; Bu, 199-201, 68-80. III dissolved in H_2O and treated with 10% NaOH to pH 7-9 gave the free amino acids (IV) (R and m.p. given): H, 280° ; Ph, 240° ; PhCH_2 , 290° (decomposition); PhCH_2CH_2 , $150-5^\circ$ (decomposition); Et, 269° ; Pr, 250° ; Bu, 181° and 290° . IV heated

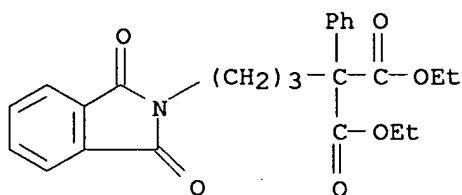
above its m.p. furnished V (R and m.p. given): H, 173°; Ph, 189-90°; PhCH₂, 134°; PhCH₂CH₂, 127-8°; Et, 124°; Pr, 102°; Bu, 69-74°; cyclohexyl, 179-80°. IV dissolved in Ae₂O, evaporated, and diluted with H₂O gave V N-Ac derivs. (VI) (same data): H, 45-6°; Ph, 94°; PhCH₂, 83°; PhCH₂CH₂, 60-1°; Et, 106-7°. VI dissolved in EtOH and alkalinized afforded V. V (R = Ph) treated with NaNH₂ in C₆H₆ and then refluxed 2-3 hrs. with MeI gave N-Me derivative of V (R = Ph), m. 119-20°; similarly, V(R = PhCH₂) gave the N-Me derivative, m. 86°. V(R = Et) with PhCH₂Cl gave N-benzyl derivative, m. 54-5°. Ethyl phenylmalonate (0.1 mole) refluxed 1 hr. with 2.3 g. Na in EtOH, cooled, and treated with γ-bromopropylphthalimide in 20 ml. HCONMe₂ and then refluxed again 4 hrs. gave Et 2-phthalimidopropyl-2-phenylmalonate (VII), m. 90°. VII refluxed with 48% HBr gave 5-phthalimido-2-phenylpentanoic acid, m. 162°. VII refluxed with 48% HBr in AcOH 60 hrs. furnished III (R = H), m. 130°. II (10 g.) (R = Ph) refluxed 3 hrs. with 30 ml. NH₂NH₂.H₂O in 100 ml. EtOH gave 86% 5-amino-2,2-diphenylpentanenitrile, b₂ 195-200°.

IT 96465-03-1, Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester

(preparation of)

RN 96465-03-1 CAPLUS

CN Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 66 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:409293 CAPLUS

DN 59:9293

OREF 59:1747f-h

TI α-Substituted δ-aminopentanoic acid

AU Salmon-Legagneur, Francois; Neveu, Cecile

CS Fac. Sci., Rennes, Fr.

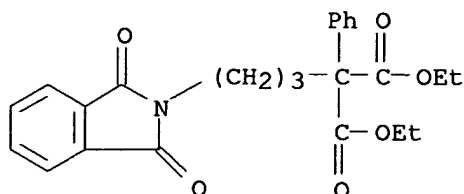
SO Compt. Rend. (1963), 256, 187-9

DT Journal

LA Unavailable

AB NH₂(CH₂)₃CPhRCO₂H (I) was prepared as the HBr salt by condensing PhRCNacN with bromopropyl-phthalimide in HCONMe₂, and refluxing the resulting 5-phthalimido-2-phenyl-2-alkylvaleronitrile (yields 55-95%) in 66% aqueous HBr and AcOH (yields 75-90%). The free amino acid was obtained by neutralizing with NaOH. The lactams were also prepared by heating the corresponding amino acid. The following I were prepared (R, and m.p. of I, the HBr salt, and the lactam given): H, 280°, 130°, 173°; Et, 269°, 161°, 124°; Pr, 204°, 178°, 102°; Bu, 295°, 199-201°, -- (the lactam was not obtained); Ph, 240°, 260°, 189-90°; PhCH₂, 290°, 174°, 134°; PhCH₂CH₂, 150-55° (decomposition), 214°, 127-8°.

IT 96465-03-1, Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester
 (preparation of)
 RN 96465-03-1 CAPLUS
 CN Malonic acid, phenyl(3-phthalimidopropyl)-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 67 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:8783 CAPLUS

DN 58:8783

OREF 58:1435d-h

TI α -Substituted carboxylic acids

IN LIPHA; Szarvasi, Etienne; Newvy, Liliane; Fontaine, Louis

PA Lyonnaise Industrielle Pharmaceutique

SO 40 pp.

DT Patent

LA Unavailable

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------|------|----------|-----------------|------|
| PI | BE 613547 | | 19620806 | BE | <-- |
| | FR AD81162 | | | FR | |
| PRAI | FR | | 19620223 | | |

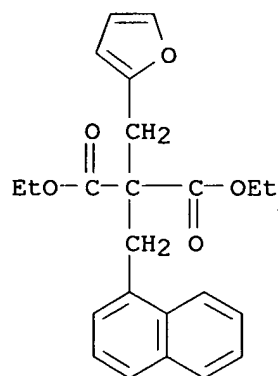
AB Compds. of the general formula $RR'CHOR''$ (I), where COR'' can be an acid, ester, acid salt, or amide group, can be used to induce cholesterolemia; they have choleretic properties. Na (9 g.) is placed in 256 ml. absolute EtOH, 96 g. Et furfurylmalonate added, the mixture boiled 5 min., cooled, 70.4 g. 1-C10H7CH2Cl added dropwise, the mixture refluxed 24 hrs., extracted with C6H6, and the extract distilled to give 69% Et α -(1-naphthylmethyl)- α -furfurylmalonate, b1.5 202-3°. Similarly prepared is Et (1-naphthylmethyl)tetrahydrofurfurylmalonate, b0.95 211°. C10H7CH2CN is refluxed with NaNH2 and furfuryl chloride 6 hrs. to give α -(1-naphthyl)- α -furfurylacetonitrile, b2 194-5°, n22D 1.611, m. 46-8° (EtOH-C6H14). Similarly prepared are the following $RR'CHCN$ (R-, R', b.p. given): 1-C10H7, tetrahydrofurfuryl, b0.4 154°; 1-C10H7, 3-tetrahydrofurfuryl, propyl, b0.4 183°; 1-C10H7, MeCH:CHCH2, b0.9 138°; 1-C10H7, H2C:CHCH2, b0.4 130°, n19.5D 1.603, d21 1.0520. I prepared were [R, R', R'', and phys. properties given]: 1-C10H7CH2, furfuryl, OH, m. 72-4°, b1.5 207-9° (Na salt m. 260-2°); 1-C10H7CH2, furfurylmethyl, OMe, b2 193-5°, d25 1.1333, n23D 1.583; 1-C10H7CH2, furfuryl, tert-BuCH2O, b2 179-80°, n23.5D 1.5585; 1-C10H7CH2, furfuryl, OCH2CH2NEt2, b1 188-90°, n21D 1.5728; 1-C10H7CH2, 3-tetrahydrofurfurylpropyl, OH, b1 220-2° (Na salt m. 261°); 1-C10H7CH2, 3-tetrahydrofurfurylpropyl, OMe, b0.6 178°, d24 1.182; 1-C10H7, furfuryl, OH, b2 218-19°, m. 80-2° (Na salt m. 302-3°); 1-C10H7, furfuryl, NH2, m. 107-8° (EtOH); 1-C10H7, furfuryl, OMe, b0.7 158°, d24 1.1375, n23D 1.596; 1-C10H7,

furfuryl, tert-BuCH₂O, b1 171-2°, n₂₁D 1.561; 1-C10H7, furfuryl, OCH₂CH₂NEt₂, b1.5 215-16°, n₂₄D 1.5745; 1-C10H7, furfuryl, NHCH₂CH₂OH, m. 122-3° (EtOAc and EtOH); 1-C10H7, tetrahydrofurfuryl, OH, b1.5 217-18°, m. 135° (EtOH-C₆H₁₄) (Na salt m. 250-1°); 1-C10H7, tetrahydrofurfuryl, NH₂, m. 153-3.5° (EtOAc); 1-C10H7, tetrahydrofurfuryl, OMe, b0.36 157-8°; 1-C10H7, tetrahydrofurfuryl, tert-BuCH₂O, b1 182-5°; 1-C10H7, tetrahydrofurfuryl, OCH₂CH₂NEt₂, b0.36 191°; 1-C10H7, 3-tetrahydrofurylpropyl, OH, b0.35 210°; 1-C10H7, 3-tetrahydrofurylpropyl, O(CH₂)₂NEt₂, b0.6 216°, n₂₂D 1.5555; 1-C10H7CH₂, tetrahydrofurfuryl, OH, b1 212°; 1-C10H7, MeCH:CHCH₂OH, b0.7 167°; 1-C10H7, MeCH:CHCH₂, NH₂, m. 121-2° (EtOAc); 1-C10H7, MeCH:CHCH₂, OMe, b1 131-4° d₂₂ 1.0616, n₂₂D 1.5825; 1-C10H7, MeCH:CHCH₂, O(CH₂)₂NEt₂, b2 197°, d₂₂ 1.020, n₂₂D 1.564; 1-C10H7, MeCH:CHCH₂, NHNH₂, m. 125-7° (EtOAc), sublimation at 100°; 1-C10H7, H₂C:CHCH₂, OH, b0.6 157-8°; 1-C10H7, H₂C:CHCH₂, O(CH₂)₂NEt₂, b1 148-9°, d₂₃ 1.0205, n₂₄D 1.555; 1-C10H7, H₂C:CHCH₂, O(CH₂)₂NMe₂, b1 166-8°.

IT 95432-29-4, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester
(preparation of)

RN 95432-29-4 CAPLUS

CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester
(9CI) (CA INDEX NAME)



L5 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:483159 CAPLUS

DN 57:83159

OREF 57:16563d-i

TI α-Substituted carboxylic acids

IN Szarvasi, Etienne; Neuvi, Liliane

PA LIPHA; Lyonnaise Industrielle Pharmaceutique

SO 29 pp.

DT Patent

LA Unavailable

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|-----------------|--------------|
| PI | FR 1289597 | | 19620406 | FR | 19610223 <-- |
| | GB 999589 | | | GB | |
| | GB 999590 | | | GB | |
| | US 3257420 | | 1966 | US | <-- |

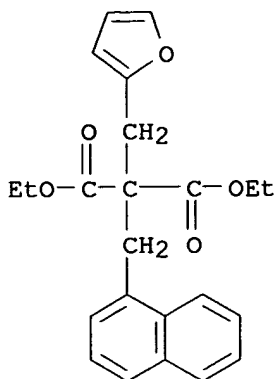
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|------------|------|----|-----|
| US 3282964 | 1966 | US | <-- |
| US 3282965 | 1966 | US | <-- |

AB The Na salts, esters, and amides of R'R''C(CO₂R)₂ (I), RCH₂CHR'CN (II), and R'R''CHCO₂R (III) show choleretic and hypocholesterolemic properties. NaOEt (9 g.) in 256 ml. absolute EtOH is prepared, 96 g. ethyl furfurylmalonate added, the mixture boiled 5 min., cooled, 70.4 g. 1-chloromethylnaphthalene added dropwise, the mixture refluxed 24 hrs., extracted with C₆H₆, and distilled to give 105 g. I (R = Et, R' = furfurylmethyl, R'' = 1-C₁₀H₇CH₂), b₁.5 202-3°. Similarly prepared are: I [R = Et, R' = 3-(tetrahydrofurfuryl)propyl, R'' = 1-C₁₀H₇CH₂], b₀.95 211°, 64% yield; II (R = furfurylmethyl, R' = 1-C₁₀H₇), b₂ 194-5°, n₂₂D 1.611, 71.8%, m. 46.5-8° (EtOHC₆H₁₄); II (R = tetrahydrofurfuryl, R' = 1-C₁₀H₇), b₀.4 154°, 67%; II [R = 2-(tetrahydrofurfuryl)ethyl, R'' = 1-C₁₀H₇], b₀.4 183°, 60%; II (R = 1-propenyl, R' = 1-C₁₀H₇), b₀.9 138°, 65.7%; II (R = vinyl, R' = 1-C₁₀H₇), b₀.4 130°, n₁₉.5D 1.603, d₂₁ 1.0520, 85.6%; II (R = HC:C, R' = 1-C₁₀H₇), b₁ 156°, n₁₈D 1.615, m. 63-7° (EtOAc), 32%; III (R = H, R' = furfurylmethyl, R'' = 1-C₁₀H₇CH₂), b₁.5 207-9°, m. 72-4° (EtOAc-C₆H₁₄), 72%; III (R = Me, R' = furfurylmethyl, R'' = 1-C₁₀H₇CH₂), b₂ 193-5°, d₂₅ 1.3333, n₂₃D 1.583; III (R = CH₂CH₂NEt₂, R' = furfurylmethyl, R'' = 1-C₁₀H₇CH₂), b₁ 188-90°, n₂₁D 1.5728, 60.5%; III [R = H, R' = 3-(tetrahydrofurfuryl)propyl, R'' = 1-C₁₀H₇CH₂], b₁ 220-2°, 77%, m. 261° (R = Na, decomposition); III [R = Me, R' = 3-(tetrahydrofurfuryl)propyl, R'' = 1-C₁₀H₇CH₂], b₀.6 178°, d₂₄ 1.182, 57.7%; III (R = H, R' = furfuryl, R'' = 1-C₁₀H₇), b₂ 218-19°, m. 80-2° (EtOAc-C₆H₁₂), 71.3%, m. 302-3° (Na salt, H₂O); III [(CO₂R =)CONH₂ R' = furfuryl, R'' = 1-C₁₀H₇], m. 107-8° (EtOH), 30.2%; III (R = Me, R' = furfuryl, R'' = 1-C₁₀H₇), b₀.7 158°, d₂₄ 1.1375, n₂₃D 1.596, 67%; III (R = CH₂CH₂NEt₂, R' = furfuryl, R'' = 1-C₁₀H₇), b₁.5 215-16°, n₂₄D 1.5745, 46%; III (R = H, R' = tetrahydrofurfuryl, R'' = 1-C₁₀H₇), b₁.5 217-18°, m. 135° (EtOAc-C₆H₁₄), 66.5%; III [(CO₂R =)CONH₂, R' = tetrahydrofurfuryl, R'' = 1-C₁₀H₇], m. 153-3.5° (EtOAc), 75%; III (R = Me, R' = tetrahydrofurfuryl, R'' = 1-C₁₀H₇), b₀.36 157-8°, 75.5%; II (R = Et₂NCH₂, R' = tetrahydrofurfuryl, R'' = 1-C₁₀H₇), b₀.36 191-4°, 51.5%; III [R = H, R' = 2-(tetrahydrofurfuryl)ethyl, R'' = 1-C₁₀H₇], b₀.35 210°, 57.5%; III (R = H, R' = MeCH:CHCH₂, R'' = 1-C₁₀H₇), b₀.7 167° [amide m. 121-2° (EtOAc), 87.7%]; III (R = H, R' = allyl, R'' = 1-C₁₀H₇), b₀.67 157-8°, 55%.

IT 95432-29-4, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester
(preparation of)

RN 95432-29-4 CAPLUS

CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester
(9CI) (CA INDEX NAME)



L5 ANSWER 69 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:475807 CAPLUS

DN 57:75807

OREF 57:15044b-i,15045a-i

TI Substituted aliphatic acids with hypocholesteremie activity

AU Szarvasi, Etienne; Neuvi, Liliane

CS Soc. Lipha, Lyon

SO Bulletin de la Societe Chimique de France (1962) 1343-54

CODEN: BSCFAS; ISSN: 0037-8968

DT Journal

LA Unavailable

AB Diethyl furfurylmalonate (140.8 g.) was heated to boiling with 14 g. Na in 400 ml. EtOH, the solution cooled, 72 g. PhCH₂Cl added, the mixture refluxed 24 hrs., poured into H₂O, worked up through C₆H₆, and the dried product fractionated to give 5.7 g. liquid, b_{2.5} 53-100°, 4.6 g. liquid, b₂ 101-59°, and 157 g. R(CH₂)_nC(CO₂Et)₂R' (I) (R = 2-furyl, R' = Ph-CH₂, n = 1) (II), b₂ 163-4°, b_{0.15} 138-40°, d₂₃ 1.095, n_{22D} 1.511. Similarly were prepared (product, % yield, b.p./mm., d./temperature,

and

nD/temperature given): I (R = 2-furyl, R' = furfuryl, n = 1) (III), 80, 148-50°/1.5 (134-7°/0.7), 1.118/20°, 1.491/17°; I (R = 2-furyl, R' = tetrahydrofurfuryl, n = 1) (IV), 60, 150-4°/3, -, -; I (R = 2-tetrahydrofuryl, R = PhCH₂, n = 3) (V), 80, 176-8°/1, 1.0640/20.5°, 1-505/18°; I (R = 2-furyl, R' = α-naphthylmethyl, n = 1) (VI), 69, 202-3°/1.5, -, -; I (R = 2-tetrahydrofuryl, R' = α-naphthylmethyl, n = 3) (VII), 65, 211°/0.95, -, -, I (R = 2-tetrahydrofuryl, R' = α-naphthylmethyl, n = 1), 78, 200°/1, -, -. In the

condensations involving furfuryl chloride (VIII) and tetrahydrofurfuryl bromide, preparation of III and IV, resp., EtOH was replaced by Et₂CO₃. II (108.8 g.) was refluxed 15 hrs. with 37.6 g. KOH in 2800 ml. PhCH₂OH, the solvent evaporated in vacuo, and the residue dissolved in H₂O. The cloudy solution was washed with Et₂O, acidified (Congo red) with HCl, extracted with C₆H₆, the extract dried, the solvent evaporated, and the residue fractionated

to

give 50 ml. PhCH₂OH, a few drops of a liquid, b_{<1} 58-150°, and 65.3 g. R(CH₂)_nCHR'CO₂H (IX) (R = 2-furyl, R' = PhCH₂, n = 1) (X), b_{<1} 152-3°, solidified to give crystals, m. 38-40° (unless otherwise stated, m.ps. were determined on a Kofler hot stage); 9.7 g. crude X recrystd. from 30 ml. pentane (refrigerator) and dried in vacuo gave X, m. 40-3° (capillary), b_{0.8} 143-4°; X Na salt (XI) m.

253-4° (capillary). Similarly were prepared (starter, product, % yield, b.p./mm., m.p., and m.p. of salt given): III, IX (R = 2-furyl, R' = furfuryl, n = 1) (XII), 72, 141-3°/1, 56-8° (AcOH), Na salt (XIII) 220-2° (decomposition) (capillary); IV, IX (R = 2-furyl, R' = tetrahydrofurfuryl, n = 1) (XIV), 83, 163-5°/1, 79-80° (capillary) (Me₂CO), 243° (decomposition) (capillary); V, IX (R = 2-tetrahydrofuryl, R' = PhCH₂, n = 3) (XV), 86, 178-82°/1 (n_{21.5D} 1.5225), -, 230° (decomposition) (capillary); VI, IX (R = 2-furyl, R' = α-naphthylmethyl, n = 1) (XVI), 72, 207-9°/1.5, 72-4° (EtOAc-hexane), Na salt (XVII) 260-2° (capillary); VII, IX (R = 2-tetrahydrofuryl, R' = α-naphthylmethyl, n = 3) (XVIII), 81, 220-2°/1, -, Na salt (XIX) 261 (decomposition) (capillary) (hygroscopic). XII (22 g.) in 100 ml. dry C₆H₆ refluxed 8.5 hrs. with 8.5 g. piperidine (XX) and the C₆H₆ evaporated gave 26.5 g. crude XII piperidinium salt (XXI), m. 96-8° (capillary) (EtOAc). Similarly, X gave X piperidinium salt (XXII), m. 102-3° (capillary) (EtOAc), in 100% yield. α-Naphthylacetonitrile (196 g.) was refluxed 1 hr. with 58 g. 90% NaNH₂ in 580 ml. Et₂O, 157 g. VIII in 157 ml. Et₂O then added, reflux continued 6 hrs., and the mixture worked up to give 208 g. R(CH₂)_nCHR'CN (R' = α-naphthyl) (XXIII) (R = 2-furyl, n = 1) (XXIV), b_{0.5} 164-6°, n_{22D} 1.611, m. 46.5-8.0° (EtOH-hexane). Similarly were prepared product, % yield, b.p./mm., and m.p. given): XXIII (R = 2-tetrahydrofuryl, n = 1) (XXV), 67, 184-7°/1 (154°/0.4), 44-6° (EtOH-hexane); XXIII (R = 2-tetrahydrofuryl, n = 3) (XXVI), 69, 182-4°/0.5, -; XXIII (R = MeCH:CH, n = 1) (XXVII), 82, 147-9°/0.4, -; XXIII (R = CH₂:CH, n = 1) (XXVIII), 86, 132°/0.5 (d₂₁ 1.0520, n_{19.5D} 1.603), -; XXIII (R = CH.tplbond.C, n = 1), 32, 156°/1 (n_{18D} 1.615), 63-7° (EtOH). XXIV (79 g.) refluxed 15 hrs. with 20 g. KOH in 1660 ml. PhCH₂OH and worked up as above gave 56.5 g. IX (R' = α-naphthyl) (XXIX) (R = 2-furyl, n = 1) (XXX), b₂ 218-19°, which solidified when rubbed with a glass rod, m. 84.5-5.5° (EtOAc-hexane); Na salt (XXXI) m. 302-3°. Similarly were prepared (starter, product, % yield, b.p./mm., m.p., and m.p. of salt given): XXV, XXIX (R = 2-tetrahydrofuryl, n = 1) (XXXII), 67, 217-18°/1.5, 135°, Na salt (XXXIII) 250-1° (capillary); XXVI, XXIX (R = 2-tetrahydrofuryl, n = 3) (XXXIV), 75, 210°/0.35, -, Na salt (XXXV) - (hygroscopic); XXVII, XXIX (R = MeCH:CH, n = 1) (XXXVI), 79, 167°/0.7, -, Na salt (XXXVII) - (hygroscopic); XXVIII, XXIX (R = CH₂:CH, n = 1), 65, 157-8°/0.6, 84-7° (EtOAc-hexane), Na salt (XXVIII) - (hygroscopic). Neopentyl esters were prepared by azeotropic distillation in C₆H₆; other esters were prepared by treatment of the acid with excess boiling alc. Thus were prepared (acid, ester, % yield, b.p./mm., d./temperature, and nD/temperature

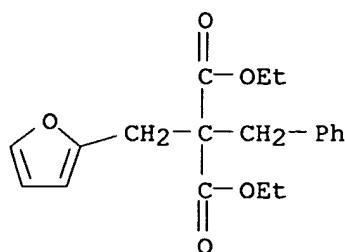
given): X, Me (XXXIX), 87.5, 121-2°/1, 1.0783/20°, 1.5265/19°; X, neopentyl, 46, 166°/2, 1.006/23°, 1.5072/20°; X, tert-Bu, 47.5, 122°/1, 1.0019/25°, 1.505/24°; XII, Me (XL), 82, 100-2°/1, 1.111/19.5°, 1.515/18°; XII, neopentyl, 70, 114°/1, 1.0290/25°, 1.486/24°; XII, tert-Bu, 45, 116°/1, 1.021/23.5°, 1.484/23°; XIV, Me (XLI), 84.5, 131.5°/2.5, 1.0703/22°; XIV, neopentyl, 40, 127°/1, 1.007/25°, 1.4765/25°; XIV, tert-Bu, 66, 120°/1, 1.003/24°, 1.4737/23°; XV, Me (XLII), 89, 154-5°/2, 1.023/21°, 1.507/21°; XV, neopentyl, 67, 156°/1, 0.971/23°, 1.4955/22°; XV, tert-Bu, 44, 163°/2, 0.9839/22°, 1.4958/20°; XVI, Me (XLIII), 74, 193-5°/2,

1.1333/25°, 1.583/23°; XVI, tert-Bu (XLIV), 32, 179-80°/2, -, 1.5585/23.5°; XVIII, Me (XLV), 88, 178°/0.6, 1.182/24°, -; XXX, Me (XLVI), 67, 158°/0.7, 1.1375/24°, 1.596/23°; XXX, tert-Bu (XLVII), 49, 171-2°/1, 1.0652/21°, 1.561/21°; XXXII, Me (XLVIII), 76, 157-8°/ 0.36, -, -; XXXII, tert-Bu (XLIX), 59, 182-5°/1, -, 1.551/ 20°; XXXIV, Me (L), 79, 17.9-9.5°/1, -, -; XXXVI, Me (LI), 75, 131-4°/1, 1.0616/22°, 1.5825/22°. XL (32 g.) was refluxed 7 hrs. with 12.2 g. XX and 0.4 ml. AcOH, excess XX removed in vacuo, the cooled residue rubbed with a glass rod, and left overnight in the refrigerator to give 14 g. XXI and 6.5 g. unchanged XL. Similarly, XXXIX gave 63% XXII. XL (40 g.), 21.3 g. HOCH₂CH₂NH₂, 17 ml. PrOH, and 0.4 ml. AcOH were refluxed 16 hrs., the mixture evaporated to dryness in vacuo, the residue left overnight in the refrigerator, stirred with hexane, and filtered to give 40.5 g. N-CH₂CH₂OH amide of XII, m. 76-7° (EtOAc-hexane then EtOH). XL in iso-PrOH heated with aqueous NH₃ gave 38% XII amide, m. 112-13.5° (EtOAc). Similarly were prepared (starter, product, % yield, b.p./mm., and m.p. given): XXXIX, X amide, 28, -, 110-10.5° (EtOAc); XXXIX, N-CH₂CH₂OH amide of X, 68, 201°/3, 73-4° (EtOAc-hexane); XL, N-CH₂CH₂CH₂OH amide of XII, 95, -, 87-8° (EtOAc); XLI, N-CH₂CH₂OH amide of XIV, 79, 210-12°/2 (d₂₆ 1.1254, n_{24D} 1.514), -; XLII, XV amide, 15, -, 107-8° (EtOAc); XLVI, N-CH₂CH₂OH amide (LII) of XXX, 88, -, 122-3° (EtOH). XXIV (19.5 g.) was refluxed 50 hrs. with 4.4 g. KOH in 5 ml. H₂O and 120 ml. EtOH, the EtOH evaporated, the cooled residue acidified with HCl, and worked up through Et₂O to give 105 g. XXX amide (LIII), m. 107-8° (EtOH). Similarly were prepared (starter, product, % yield, and m.p. given): XXV, XXXII amide (LIV), 75, 153-3.5° (EtOAc); XXVI, XXVI amide (LV), 88, 121-2° (sublimed) (EtOAc). XVI - XIX, XXX - XXXVII, and XLIII - LV showed hypocholesteremic activity in the Triton test, XXXI being the most active and having L. D.₅₀ 320 and 1250 mg./kg. mouse by intraperitoneal and oral administration, resp. The activity was decreased by saturation of the furan ring or increase in the length of the aliphatic chain, and lost entirely by replacement of the naphthalene system by a benzene ring. Replacement of the furan ring by an unsatd. aliphatic chain strongly decreased hypocholesteremic and hypolipemic activity, e.g. XXXVII, or if hypolipemic activity was largely retained, the hypocholesteremic activity was totally lost, e.g. XXXVIII. XXI and XXII had antiinflammatory activity against the edema produced on the paw of the rat by serotonin, and were 3 and 1.5 times as active, resp., as aspirin. XI and XIII had noteworthy choleretic activity.

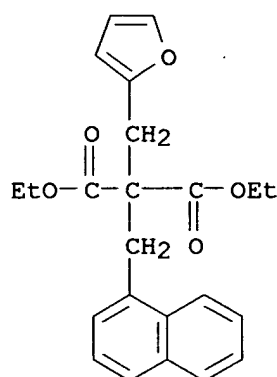
IT 94385-69-0, Malonic acid, benzylfurfuryl-, diethyl ester
 95432-29-4, Malonic acid, furfuryl(1-naphthylmethyl)-, diethyl ester

(preparation of)

RN 94385-69-0 CAPLUS
 CN Malonic acid, benzylfurfuryl-, diethyl ester (7CI) (CA INDEX NAME)



RN 95432-29-4 CAPLUS

CN Propanedioic acid, (2-furanylmethyl)(1-naphthalenylmethyl)-, diethyl ester
(9CI) (CA INDEX NAME)

L5 ANSWER 70 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:462656 CAPLUS

DN 57:62656

OREF 57:12435h-i,12436a-e

TI Aliphatic acids disubstituted by cyclic radicals

IN Szarvasi, Etienne; Neuvy, Liliane

PA LIPHA (Lyonnaise Industrielle Pharmaceutique)

SO 12 pp.

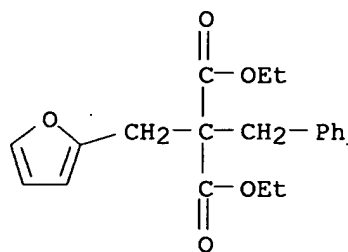
DT Patent

LA Unavailable

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | FR 1278631 | | 19620322 | FR | 19600729 <-- |
| AB | The preparation of acids with the general formula $R_1CH_2CH[R_2(CH_2)_n]CHCO_2H$ ($n = 1$ or 3 , $R_1 = Ph$, furyl, or tetrahydrofuryl for $n = 1$, and Ph for $n = 3$, $R_2 =$ furyl for $n = 1$, and tetrahydrofuryl for $n = 3$) and derivs. as esters of primary alcs. with 1-5 C, Na, and piperidine salts, primary and secondary amines, hydrazides, and 2-aminoethanol derivs. is described. These products are of therapeutic value. Thus e.g. 140.8 g. 2-furfurylethyl malonate was added to 400 ml. EtOH containing 14 g. Na and heated to boiling. After cooling, 72 g. $PhCH_2Cl$ was added and the mixture refluxed 24 hrs., thrown into H_2O , and extracted with C_6H_6 to give 157 g. Et α -benzyl- α -furylmalonate, b_2 163-4°, d_{234} 1.095, n_{22D} 1.511. Similarly described is the preparation of Et α -difurfurylmalonate, $b_{0.7}$ 134-7°, d_{204} 1.118, n_{17D} 1.491; Et | | | | |

α -furfuryl- α -tetrahydrofurfurylmalonate, b3 150-4°; Et α -benzyl- α -(tetrahydrofurylpropyl)malonate, b1 176-8°, d20.5D 1.0640, n18D 1.505; β -phenyl- β' -furylisobutyric acid, m. 40-3° (Na salt decomposed at 253-4°); β, β' -difurylisobutyric acid, m. 56-8° (AcOH) (Na salt decomposed at 220-2°); β -tetrahydrofuryl- β' -furylisobutyric acid, m. 79-80° (Na salt decomposed at 243°); α -benzyl- δ -tetrahydrofurylvaleric acid, b1 178-82°, n21.5D [Na salt m. 230° (decomposition)]; Me β -phenyl- β' -furylisobutyrate, b. 121-2°, d204 1.0783, n19D 1.5265; isoamyl β -phenyl- β' -furylisobutyrate, b2 166°, d234 1.006, n20D 1.5072; N-diethylaminoethyl β -phenyl- β' -furylisobutyrate, b1 154-5°, d24.54 1.0541, n24.5D 1.525; neopentyl β -phenyl- β' -furylisobutyrate, b1 122°, d254 1.0019, n24D 1.505; methyl β, β' -difurylisobutyrate, b1 100-2°, d19.54 1.111, n18D 1.515; isoamyl β, β' -difurylisobutyrate, b1 114°, d234 1.0290, n24D 1.486; N-diethylaminoethyl β, β' -difurylisobutyrate, b1.5 145.5-8.0°, d23.54 1.0381, n22D 1.493; neopentyl β, β' -difurylisobutyrate, b1 116°, d23.54 1.021, n23D 1.484; methyl β -tetrahydrofuryl- β' -furylisobutyrate, b2.5 131.5°, d224 1.0703, n21D 1.486; isoamyl β -tetrahydrofuryl- β' -furylisobutyrate, b1 127°, d254 1.007, n25D 1.4765; N-diethylaminoethyl β -tetrahydrofuryl- β' -furylisobutyrate, b1 164°, d224 1.0730, n21D 1.4975; neopentyl β -tetrahydrofuryl- β' -furylisobutyrate, b1 120°, d244 1.003, n23D 1.4737; Me α -benzyl- δ -tetrahydrofurylvalerate, b2 154.5°, d214 1.023, n21D 1.507; isoamyl α -benzyl- δ -tetrahydrofurylvalerate, b1, 156°, d234 0.971, n22D 1.4955; N-diethylaminoethyl α -benzyl- γ -tetrahydrofurylvalerate, b1 178°, d214 1.028, n21D 1.5135; neopentyl α -benzyl- δ -tetrahydrofurylvalerate, b2 163°, d224 0.9839, n20D 1.4958; piperidine β -phenyl- β' -furylisobutyrate, m. 102-3°; β -phenyl- β' -furylisobutyramide, m. 109-10° (EtOAc); β -phenyl- β' -furylisobutyrylhydrazine, m. 89-91° (EtOAc); 2-(β -phenyl- β' -furylisobutyramido)ethanol, m. 73-4° (EtOAc-C6H14); piperidine β, β' -difurylisobutyrate, m. 96-8° (EtOAc); β, β' -difurylisobutyramide, m. 112-14° (EtOAc); β, β' -difurylisobutyrylhydrazine, m. 96.5-7.5° (EtOAc); 2-(β, β' -difurylisobutyramido)ethanol, m. 76-7° (EtOH); β -tetrahydrofuryl- β' -furylisobutyrylhydrazine m. 66-8° (EtOAc); 2-(β -tetrahydrofuryl- β' -furylisobutyramido)ethanol, b2 210°, n264 1.1254, n24D 1.514; and α -benzyl- δ -tetrahydrofurylvalerylhydrazine, m. 71.5-2.0° (EtOAc).

IT 94385-69-0, Malonic acid, benzylfurfuryl-, diethyl ester
 (preparation of)
 RN 94385-69-0 CAPLUS
 CN Malonic acid, benzylfurfuryl-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 71 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:73488 CAPLUS

DN 56:73488

OREF 56:14281a-i,14282a-c

TI Pyridylethylbarbituric acids

AU Shapiro, Seymour L.; Bandurco, Victor; Freedman, Louis

CS U.S. Vitamin & Pharm. Corp., Yonkers, NY

SO Journal of Organic Chemistry (1962), 27, 174-8

CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA Unavailable

OS CASREACT 56:73488

GI For diagram(s), see printed CA Issue.

AB Several 5-pyridylethylbarbituric acids (I), with markedly increased hexobarbital (II) sleeping time, were synthesized. The requisite intermediates were obtained from the corresponding picolyl chloride and the substituted di-Et malonate or by pyridylethylation of the malonate ester. Na (6.6 g.) in 100 ml. alc. refluxed 2.5 hrs. with 26.4 g. EtCH(CO₂Et)₂ and 22.8 g. 2-C₅H₄NCH₂Cl.HCl, the cooled mixture treated with 100 ml. H₂O and 10 ml. HCl, the alc. evaporated, the solution washed with Et₂O, treated with 50 ml. 10% aqueous NaOH, extracted with 150 ml. Et₂O, and the residue

on evaporation of the H₂O washed extract distilled yielded 18% product (III).

Na

(3.0 g.) in 100 ml. alc. refluxed 6 hrs. with 44.0 g. 4-C₅H₄NCH: CH₂, 100 g. EtCH(CO₂Et)₂, and 0.1 g. hydroquinone, the alc. evaporated, the residue diluted with 200 ml. H₂O and 56 ml. HCl, washed with Et₂O, treated with 100 ml. 20% aqueous NaOH, the product extracted with Et₂O, the extract washed with

H₂O

and aqueous NaHSO₃, evaporated, and the residue distilled yielded 65% ester,

b0.15

150-60°, hydrolyzed to the malonic acid, m. 146° (MeCN).

Similarly were prepared the listed intermediates, C₅H₄N(CH₂)_nCR₁(CO₂Et)₂

(position of azine N, n, R₁, b.p./mm., and % yield given): 2, 1, Et,

122-8°/0.05, 18; 3, 1, Et, 132°/0.35, 5; 4, 1, Et,

138-42°/0.3, 14; 2, 2, H, 130-4°/0.1, 26; 2, 2, Et,

150-60°/0.15, 65; 2, 2, Et, 150-2°/0.6, 16; 2-(5-EtC₅H₃N),

2, Et, 160-8°/0.3, 41; 4, 2, H, 140-2°/0.3, 5; 4, 2, Me

(IV), 140-50°/0.1, 37; 4, 2, Et, 150-8°/0.45, 50. NaOH (1.8

g.) and 8 g. (4-C₅H₄NCH₂CH₂)CPh(CO₂Et)₂ refluxed 2 hrs. in 20 ml. H₂O, the cooled solution diluted with 50 ml. H₂O, treated with 4.3 ml. HCl, extracted

with

warm CHCl₃ (50 ml.), and the product recrystd. from dilute alc. yielded 7%

4-C₅H₄NCH₂CH₂CHPhCO₂H, m. 125-7°. Na (1.0 g.) in 20 ml. alc.

treated with 6.0 g. (α-C₅H₄NCH₂)CET(CO₂Et)₂ and 1.6 g. (H₂N)₂CO in

10 ml. hot alc., the mixture refluxed 6 hrs., the cooled solution diluted with 100 ml., the alc. evaporated, and the Et₂O-washed residue neutralized yielded 48% I (R = H, R₁ = α -C₅H₄NCH₂, R₂ = Et), m. 230-2° (BuOH).

Similarly were prepared compds. 2 and 3, I (R = H, R₁ = β - and γ -C₅H₄NCH₂, R₂ = Et), m. 220°, and 234-5°, resp. Na

(1.0 g.) in 20 ml. alc., 7 g. (4-C₅H₄NCH₂CH₂)CMe (CO₂Et)₂, and 1.9 g.

(H₂N)₂CS in 20 ml. hot alc. refluxed 9 hrs., the cooled solution diluted with 100 ml. H₂O, the alc. evaporated, and the Et₂O-washed aqueous residue adjusted

to

pH 7 yielded 61% compound 21, m. 220-30°. For the 2-imino barbituric acids, an addnl. equivalent of Na alkoxide liberated (H₂N)₂C:NH from its HCl salt. Employing the appropriately substituted malonate and urea, similarly were prepared the listed compds. 4-35 [series (R₁ and R₂), number, R, X (if other than O), and m.p./solvent given]. 2-C₅H₄NCH₂CH₂, Et: 4, H, 205°/PrOH; 5, H, S, 217-19°/PrOH; 6, H, NH, above 300°/AcOH-MeCN (dipicrate m. 238-40°/alc.); 7, Me, 150-3°/alc.; 8, Et, 123-4°/alc.; 9, H₂C:CHCH₂, 120°/MeCN; 10, Bu, 85°/alc.; 11, Ph, 185-7°/alc. 2-(5-EtC₅H₃N)CH₂CH₂, Et: 12, H, 220-2°/MeCN; 13, H, S, 201-2°/MeCN; 14, H, NH, 280° (decomposition)/AcOH-alc.; 15, Me, 154°/alc.; 16, Et, 137-8°/alc.; 17, H₂C:CHCH₂, 127-8°/MeCN; 18, Bu, 80-1°/Et₂O-C₆H₁₄; 19, Ph, 166-7°/alc. 4-C₅H₄NCH₂CH₂, Me: 20, H, 252-4°/MeOH; 21, H, S, 227-30°/PrOH; 22, H, NH, over 300°/MeOH; 23, Me, 204-6°/alc.; 24, Et, 176-7°/MeCN; 25, Bu, 174-5°/alc.; 26, Ph, 125-6°/MeOH. 4-C₅H₄NCH₂CH₂, Et: 27, H, 224-6°/MeCN; 28, H, S, 224-6°/PrOH; 29, H, NH, above 300°/PrOH (di-HCl salt m. 210-12°/alc.); 31, Me, 148-50°/alc.; 32, Et, 110°/alc.; 33, H₂C:CHCH₂, 115°/MeCN; 34, Bu, 102-4°/Et₂O-C₆H₁₄; 35, Ph, 177-8°/alc. No critical stage was noted with pyridylethyl substituents and average yields of 26-29% were noted. As R₁ was varied from H, Me, Et, C₃H₅ Bu, and Ph (X = O), average yields of 20, 24, 41, 14, 30, and 33%, resp., were obtained. Na (1.2 g.) in 50 ml. alc. and 2.6 g. (H₂N)₂CO in 20 ml. alc. refluxed 7 hrs. with 17.6 g. (2-C₅H₄NCH₂CH₂)CPh(CO₂Et)₂, the cooled mixture diluted with 100 ml. H₂O, the alc.-free aqueous residue

extracted

with 100 ml. Et₂O, and neutralized yielded 11% 2-C₅H₄NCH₂CH₂CHPhCONH₂, m. 121-3° (alc.). The Et₂O extract evaporated and the residue crystallized gave 0.5 g. 2-C₅H₄NCH₂CH₂CHPhCO₂H, 161-2° (alc.). Treatment of 3.9 g.

5-ethylbarbituric acid in 100 ml. alc. with 5.2 g. 4-C₆H₄NCH:CH₂ (exothermic reaction) and recrystn. of the product yielded 40% compound 27, mixed m.p. 224-6°. Similarly, 1 g. 5-phenylbarbituric acid and 0.5

g. 4-C₅H₄NCH:CH₂ in 25 ml. hot 1:1 H₂O-alc. evaporated on a steam bath and the precipitate recrystd. from 35 ml. 6:1 H₂O-alc. yielded 47% of the otherwise inaccessible I (R = H, R₁ = 4-C₅H₄NCH₂CH₂, R₂ = Ph), compound number 36, m.

248-9°. The effects of structure on the ultraviolet absorption spectra and the pK_a were noted, discussed, and the measurements tabulated.

The compds. were without substantial toxicity or central nervous system depressant effects. The most conspicuous effect was enhancement of II sleeping time, particularly with compound 31, which showed a 420% increase. The (4-pyridyl)ethyl compds. showed greater effects than the 2-congeners.

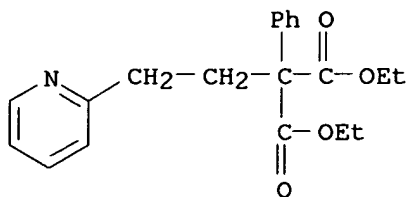
IT 94577-33-0, Malonic acid, phenyl[2-(2-pyridyl)ethyl]-, diethyl ester 94577-34-1, Malonic acid, phenyl[2-(4-pyridyl)ethyl]-, diethyl ester

(preparation of)

RN 94577-33-0 CAPLUS

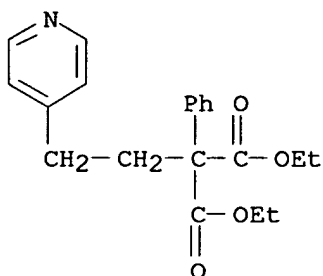
CN Malonic acid, phenyl[2-(2-pyridyl)ethyl]-, diethyl ester (7CI) (CA INDEX

NAME)



RN 94577-34-1 CAPLUS

CN Malonic acid, phenyl[2-(4-pyridyl)ethyl]-, diethyl ester (7CI) (CA INDEX NAME)



L5 ANSWER 72 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1962:2254 CAPLUS

DN 56:2254

OREF 56:424f-h

TI N-Substituted acid amides

IN Boehme, Horst; Eiden, Fritz

PA Farbwerke Hoechst A.-G.

DT Patent

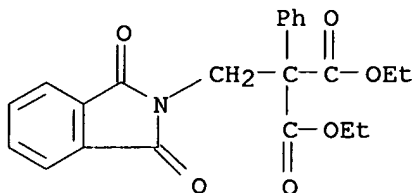
LA Unavailable

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | | |
|----|------------|--|----------|----|-----|
| PI | DE 1096360 | | 19610105 | DE | <-- |
|----|------------|--|----------|----|-----|

AB N-Chloromethylimides treated with compds. containing a C with a single H in the presence of cyano, carbalkoxy, carbaryloxy, aldehydo, acetal or acyl groups gave good yields of N-substituted imides. o-C6H4-(CO)2NCH2Cl (I.) (1.9 g.) suspended in 10 g. dry Et2O added to NaCMe(CO2Et)2 (II) suspended in 20 g. Et2O yielded under reflux 3 hrs., a slimy precipitate which, washed with Et2O, and freed of Et2O yielded 2.7 g. o-C6H4(CO)2NCH2CMe(CO2Et)2, m. 96° (iso-Am2O). I treated with NaCNHAc(CO2Et)2, NaCet(CO2Et)2, NaCPh(CN)Ac, NaCMe(CO2Et)Ac, NaCMe(Bz)Ac, and NaCPh(CO2Et)2 yielded, resp. 60% RCMe(CO2Et)2 [R = o-C6H4(CO)2NCH2], m. 138° (dilute alc.); 67% RCet(CO2Et)2, m. 89° (alc.H2O); 72% RCPH(CN)Ac, m. 139° (alc.); 63% RCMe(CO2Et)Ac, plates, m. 107° (dilute alc.); 54% RCMe(Bz)Ac, m. 169° (alc.); 83% RCPH(CO2Et)2, double pyramids, m. 75-60° (MeOH). ZCH2Cl (Z = o-C6H4.SO2.N.CO) with II, and with NaCMe(CO2Et)CN yielded resp. 59% ZCH2-CMe(CO2Et)2, m. 94° (alc.), and 61% ZCH2CMe(CO2Et)CN, m. 141° (iso-Am2O). (CH2CO)2NCH2Cl with II yielded 47% (CH2CO)2NCH2CMeCO2Et)2, b0.0(110-14°.

IT 112864-34-3, Malonic acid, phenyl(phthalimidomethyl)-, diethyl ester
 (preparation of)
 RN 112864-34-3 CAPLUS
 CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)

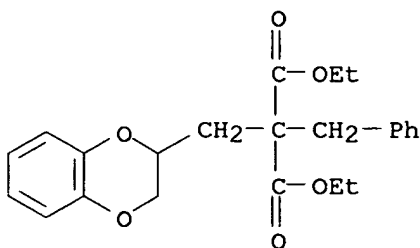


L5 ANSWER 73 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1961:27891 CAPLUS
 DN 55:27891
 OREF 55:5496d-i
 TI Benzodioxan series. XIV. 1,4-Benzodioxan-2-ylmethylmalonic and α -substituted 2-(1,4-benzodioxan)propionic acids
 AU Marini-Bettolo, G. B.; Landi-Vittory, Rodolfo; Carvalho-Ferreira, Paulo
 CS Ist. superiore sanita, Rome
 SO Gazzetta Chimica Italiana (1959), 89, 2280-90
 CODEN: GCITA9; ISSN: 0016-5603
 DT Journal
 LA Unavailable
 AB cf. CA 54, 1522e. Treatment of 1,4-benzodioxan-2-methyl bromide (QBr) (I), with NaCR(CO₂Et)₂ according to L.-V. (CA 54, 1523e) gave QCR(CO₂Et)₂ (II) together with Q₂(CO₂Et)₂ (III). Dry dioxane (15 ml.) containing 0.1 mole I refluxed (N atmospheric) and stirred with dropwise addition of NaCR(CO₂Et)₂ (0.1 mole Na and 0.13 mole RCH(CO₂Et)₂ in 20 ml. dry dioxane), the mixture refluxed 20 hrs. with stirring, the dioxane evaporated, the residue treated with H₂O, extracted with Et₂O, and the product distilled gave II (R, b.p./mm., and nD/temperature given): H, 140-50°/0.1, 1.5035/20°; Me, 114-15°/0.001, 1.4952/22°; Et, 140-50°/0.1, 1.4950/23°; Pr, 135-40°/0.03, 1.4921/22°; Me₂CH, 148-56°/0.12, 1.4969/26°; Bu, 150-5°/0.1, -; Ph, 178-80°/0.2, 65-70°, -; PhCH₂, 170-85°/0.02, 1.5299/22°. I treated with NaCH(CO₂Et)₂ gave by-product III, b0.1 210°, m. 105-10°, also produced directly from I and Na₂C(CO₂Et)₂. II (0.1 mole) refluxed 4 hrs. in 150 ml. 8% aqueous NaOH and 30 ml. alc., the cooled mixture acidified with dilute HCl, the oily product shaken with CHCl₃, extracted with dilute aqueous Na₂CO₃, acidified, and the product recrystd. from H₂O, or organic solvents gave QCR(CO₂H)₂ (IV) (R and m.p. given): Me, 164° (H₂O) [λ 278, 284 m μ (log ϵ 3.42; 3.37)]; Et, 187° (alc.); Bu, 160° (C₆H₆); PhCH₂, 168° (C₆H₆-Me₂CO). On heating above the m.p., IV gave the corresponding substituted propionic acid, QCHRCO₂H (V), also obtained by partial decarboxylation by acidification in the preparation of IV. II (0.1 mole) in 200 ml. 1:6:3 H₂O-AcOH-H₂SO₄ refluxed 10-12 hrs., diluted with 500 ml. H₂O, stirred with CHCl₃, and the H₂O-washed CHCl₃ extracted with 8% aqueous NaOH, acidified with dilute HCl, and the oily slowly-solidifying product

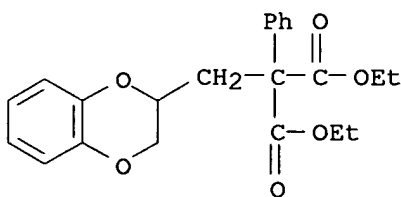
recrystd. from H₂O or organic solvents gave V [R and m.p. (solvent) or b.p./mm. given]: Me, 125° (MeOH) [λ 278, 284 m μ (log ϵ 3.36, 3.31)]; Et, 155-62°/0.6; Bu, 130-40°/0.03; Ph, 146° (MeOH) [λ 278, 284 m μ (log ϵ 3.49, 3.44)]; PhCH₂, 160-5°/0.03; H, 150° (H₂O). V (R = Ph)

obtained by acid or alkaline hydrolysis gave a mixture, which yielded a readily crystallizing form, m. 146° (MeOH), and a difficultly crystallizing isomer, m. 100° (dilute alc.), soluble in alkali and transformed by heating in H₂O to the more stable isomer. Both forms showed the same infrared spectrum in CCl₄ but presented some differences in Nujol. V provide suitable intermediates for synthesis of N derivs. in the benzodioxan series.

- IT **114842-77-2**, Malonic acid, (1,4-benzodioxan-2-ylmethyl)benzyl-, diethyl ester **116154-39-3**, Malonic acid, (1,4-benzodioxan-2-ylmethyl)phenyl-, diethyl ester
(preparation of)
RN 114842-77-2 CAPLUS
CN Malonic acid, (1,4-benzodioxan-2-ylmethyl)benzyl-, diethyl ester (6CI)
(CA INDEX NAME)

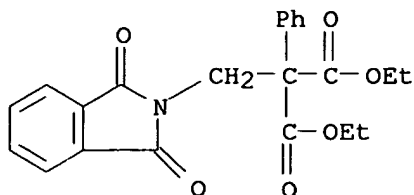


- RN 116154-39-3 CAPLUS
CN Malonic acid, (1,4-benzodioxan-2-ylmethyl)phenyl-, diethyl ester (6CI)
(CA INDEX NAME)



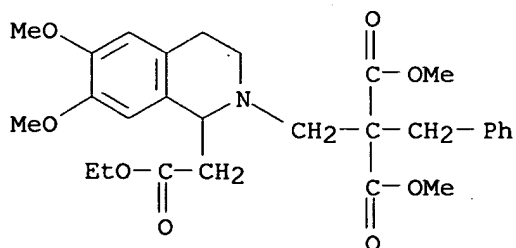
- L5 ANSWER 74 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1959:121796 CAPLUS
DN 53:121796
OREF 53:21795d-i,21796a
TI Amidomethylations of CH-acidic compounds with diacylimidochloromethanes
AU Bohme, Horst; Broese, Reinhold; Eiden, Fritz
CS Univ. Marburg, Germany
SO Chemische Berichte (1959), 92, 1258-62
CODEN: CHBEAM; ISSN: 0009-2940
DT Journal
LA Unavailable
OS CASREACT 53:121796

- AB β -Dioxo compds. which are substituted in the methylene group can be amidomethylated by reaction with diacylimidochloromethanes. Phthalimidomethanol (1.8 g.) and 2.1 g. PCl_5 each in 10-15 cc. dry Et_2O mixed, shaken, heated 10 min. on the water bath, cooled with ice- NaCl , diluted with shaking with iced H_2O , and filtered yielded 1.6 g. phthalimidochloromethane (I), m. $134-5^\circ$ (CCl_4). I (19.5 g.) in 30 cc. Et_2O added to 19.0 g. $\text{EtCH}(\text{CO}_2\text{Et})_2$ and 2.3 g. Na in 150 cc. dry Et_2O , heated 2 h. on the water bath, cooled, and diluted with H_2O , the Et_2O layer worked up, and the residue washed with petr. ether yielded 23.0 g. di-Et ethyl(phthalimidomethyl)malonate (II), m. 89° (EtOH). II (4.0 g.) and 50 cc. fuming HCl heated 2 h. in a sealed tube at 170° , cooled, filtered, and evaporated in vacuo yielded 1.5 g. $\text{H}_2\text{NCH}_2\text{CH}(\text{EtCO}_2\text{H})\cdot\text{HCl}$, m. 119° ($\text{EtOH-Et}_2\text{O}$). Na (1.4 g.) in 30 cc. absolute EtOH refluxed 6 h. with 7.0 g. II and 1.8 g. urea, cooled, concentrated on the water bath, dissolved in H_2O , and treated with HCl gave 3.5 g. 5-phthalimidomethyl-5-ethylbarbituric acid, leaflets, m. $249-51^\circ$ (hot H_2O). $\text{AcMeCHCO}_2\text{Et}$ (14.4 g.), 2.3 g. Na, and 19.5 g. I gave in the usual manner 19.0 g. di-Et methyl(phthalimidomethyl)acetoacetate, m. 107° (dilute EtOH). I (19.5 g.) and 18.1 g. $[\text{AcPhCCN}]\text{Na}$ refluxed in dry Me_2CO , cooled, and poured into H_2O yielded 23.0 g. phenyl(phthalimidomethyl)acetoacetone nitrile (III), m. 139° (EtOH). A similar run in absolute EtOH yielded 22.0 g. phenyl(phthalimidomethyl)acetone nitrile (IV), m. 124° (MeOH). IV heated 2 h. with fuming HCl yielded 86% $\text{H}_2\text{NCH}_2\text{CHPhCO}_2\text{H}\cdot\text{HCl}$, m. 201° ($\text{EtOH-Et}_2\text{O}$). BzMeCHAc (17.6 g.) treated with 2.3 g. Na, the product suspended in dry Me_2CO , the suspension refluxed 0.5 h. with 19.5 g. I, cooled, and poured into H_2O gave 18.0 g. 1-methyl-1-phthalimidomethyl-1-benzoylacetone, m. 169° (EtOH or Me_2CO). The Na salt from 7.7 g. 1,1,4-trimethyl-3,5-cyclohexanedione (V) and 9.9 g. I heated 0.5 h. in absolute EtOH on the water bath and poured into H_2O yielded 15.0 g. 4-phthalimidomethyl derivative of V, m. 159° (EtOH). Ph_2CHCHO (2.1 g.), 0.4 g. NaH , and 50 cc. dry Et_2O refluxed several hrs. with stirring, the supernatant decanted and treated with 2.0 g. I in 20 cc. dry Et_2O , the mixture heated 10 min. with stirring, and the Et_2O evaporated gave phthalimidomethyldiphenylacetaldehyde (VI), m. 99° (EtOH). VI gave with NH_2OH solution the oxime, m. 130° (EtOH). $\text{MeCH}(\text{CO}_2\text{Et})_2$ (23.6 g.) and 3.1 g. in 50 cc. dioxane added at room temperature with stirring to 20.0 g. succinimidochloromethane in 50 cc. dioxane, the dioxane evaporated in vacuo, the residue dissolved in Et_2O , and the solution washed, dried, and distilled gave 18.0 g. di-Et methyl(succinimidomethyl)malonate, viscous oil, b.p. $110-14^\circ$. By the method described for the preparation of II were obtained the following compds. (m.p., % yield, and reaction medium given): di-Et methyl(phthalimidomethyl)malonate (VII), 96° (iso- Am_2O), 81, Et_2O ; di-Et phenyl(phthalimidomethyl)malonate (VIII), $75-6^\circ$ (MeOH), 83, Et_2O ; di-Et acetamido(phthalimidomethyl)malonate (IX), 138° (aqueous EtOH), 60, absolute EtOH . VII heated with concentrated HCl and decarboxylated gave $\text{H}_2\text{NCH}_2\text{CHMeCO}_2\text{H}\cdot\text{HCl}$, m. $128-9^\circ$ ($\text{EtOH-Et}_2\text{O}$). VIII yielded similarly $\text{H}_2\text{NCH}_2\text{CHPhCO}_2\text{H}\cdot\text{HCl}$, m. 201° ($\text{EtOH-Et}_2\text{O}$), and IX gave in the same manner $\text{H}_2\text{NCH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}\cdot\text{HCl}$, m. 225° (aqueous EtOH).
- IT **112864-34-3**, Malonic acid, phenyl(phthalimidomethyl)-, diethyl ester
(preparation of)
- RN 112864-34-3 CAPLUS
- CN Propanedioic acid, [(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl-, diethyl ester (9CI) (CA INDEX NAME)



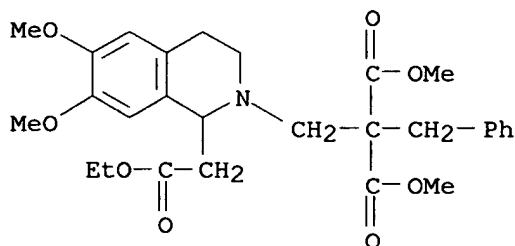
L5 ANSWER 75 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1959:51232 CAPLUS
 DN 53:51232
 OREF 53:9258f-h
 TI Halopyrazines
 IN Druey, Jean; Huni, Albrecht; Ringier, Beat H.; Staehelin, Alex
 PA C I B A Ltd.
 DT Patent
 LA Unavailable
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|------|
| PI | CH 325291 | | 19571214 | CH | <-- |
| AB | Title compds. are valuable antipyretics and are intermediates in the preparation of the medicinally useful 5,6-diamino-2-aryl-3-oxodihydropyridazines. The reaction of 5,6-dihalo-3-oxo-2,3-dihydropyridazines, having a substituted or unsubstituted aryl group in position 2 (C.A. 52, 458i), with ammonia or amines yields 5-amino-6-halo-2-aryl-3-oxo-2,3-dihydropyridazines. Thus, 14.25 g. 5,6-dichloro-2-phenyl-3-oxo-2,3-dihydropyridazine (I), m. 138°, 200 cc. EtOH, and 9 cc. morpholine refluxed 4 h. gave 6-chloro-5-morpholino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 168-9° (EtOH). I (16 g.), 200 cc. EtOH, and 12 g. piperidine refluxed 5 h. gave 6-chloro-5-piperidino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 118.5-19.5° (EtOH). I (6.4 g.) heated with 20 cc. 30% alc. Me ₂ NH solution 6 h. in a sealed tube gave 6-chloro-5-dimethylamino-2-phenyl-3-oxo-2,3-dihydropyridazine, m. 125-7° (2:1 C ₆ H ₆ -iso-Pr ₂ O). | | | | |
| IT | 117866-98-5 , Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of) | | | | |
| RN | 117866-98-5 CAPLUS | | | | |
| CN | Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME) | | | | |



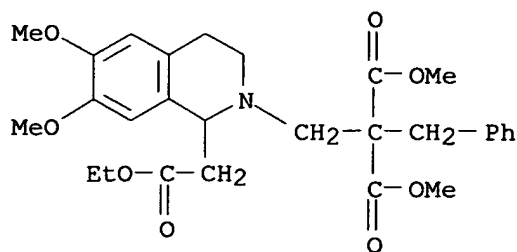
L5 ANSWER 76 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1959:51231 CAPLUS
 DN 53:51231
 OREF 53:9258f
 TI Diquaternary compounds
 IN Billinghamurst, John E. W.
 PA Wellcome Foundation Ltd.
 DT Patent
 LA Unavailable
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|------|
| PI | GB 802870 | | 19581015 | GB | <-- |
| AB | See U.S. 2,851,459 (C.A. 53, 5294g). | | | | |
| IT | 117866-98-5 , Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of) | | | | |
| RN | 117866-98-5 CAPLUS | | | | |
| CN | Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME) | | | | |



L5 ANSWER 77 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 1959:51230 CAPLUS
 DN 53:51230
 OREF 53:9258e-f
 TI 2-Oxobenzo[a]quinolizines
 IN Brossi, Arnold; Schnider, Otto; Walter, Max
 PA Hoffmann-La Roche Inc.
 DT Patent
 LA Unavailable
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|------|
| PI | US 2830993 | | 19580415 | US | <-- |
| AB | See Brit. 789,789 (C.A. 53, 4316e). | | | | |
| IT | 117866-98-5 , Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of) | | | | |
| RN | 117866-98-5 CAPLUS | | | | |
| CN | Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME) | | | | |



L5 ANSWER 78 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1959:23433 CAPLUS

DN 53:23433

OREF 53:4316d-i

TI 2-Oxobenzo[a]quinolizines

PA F. Hoffmann-La Roche & Co. Akt.-Ges

DT Patent

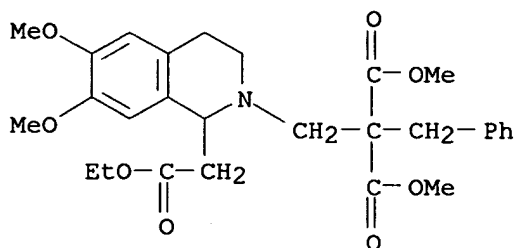
LA Unavailable

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|------|
| PI | GB 789789 | | 19580129 | GB | <-- |
| AB | <p>1-(Alkoxy carbonylmethyl)-1,2,3,4-tetrahydroisoquinoline or the 1,2,3,4,5,6,7,8-octahydro analog, both of which may contain lower (not more than 3 C) alkoxy or an alkylendioxy group at the 6 and 7 positions is condensed with formaldehyde or paraformaldehyde and malonic acid or its dimethyl ester which contains an alkyl or aralkyl group of not more than 8 C or the tetrahydrofurfuryl group. The resulting product is cyclized by heating with an alkaline condensing agent, then hydrolyzed and decarboxylated. The salt of the 2-oxo-3-substituted-1,2,3,4,6,7-hexahydrobenzo[a]quinolizine or its derivative in which the benzo moiety is partially hydrogenated and (or) contains lower alkoxy or alkylendioxy substituents at the 9 and 10 positions is converted to its free base or salts. Thus, 1-ethoxycarbonylmethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (280 g.), 35 g. paraformaldehyde, and 150 g. CH₂(CO₂Me)₂ were heated under reflux in 1000 ml. MeOH. On cooling 1-ethoxycarbonylmethyl-2-[2,2-bis(methoxycarbonyl)propyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I), m. 89-91°, crystallized Na (28 g.) was dissolved in 500 ml. MeOH, the solution evaporated to dryness, 3500 ml. toluene and 440 g. I added, and the mixture heated with stirring. After the MeOH had distilled and the b.p. of toluene was reached, the mixture was refluxed 2 hrs. and evaporated to dryness. The residue was heated under reflux for 16 hrs., cooled, and made alkaline with NH₄OH to precipitate 2-oxo-3-methyl-9,10-dimethoxy-1,2,3,4,6,7-hexahydrobenzo [a]-quinolizine (II), m. 138-40°; HCl salt, m. 204-5°. Also prepared by similar procedures were 2-oxo-3-R-substituted-9,10 - dimethoxy - 1,2,3,4,6,7 - hexahydrobenzo[a]quinolizines (R, and m.ps. base, HCl salt, and HBr salt given); Me, 138-40°, 204-5°, -, Et, 110-20°, 198-200°, 218°; iso-Pr, 123-4°, -, 222-3°; allyl, 116-17°, -, 204-5°; Bu, 112-14°, 188-9°, -, benzyl, 139-41°, 165-7°, -, iso-Bu, 126-8°, 196-7°, -, Am, 121-2°, 184-5°, -, hexyl, 92-4°, 173-5°, -. Also prepared similarly were 2-oxo-3-ethyl-1,2,3,4,6,7,8,9,10,11-decahydrobenzo[a]quinolizine, m. 69° (HCl salt, m. 122°);</p> | | | | |

2-oxo-3-ethyl-9,10-methylenedioxybenzo-[a]quinolizine, m. 147-9° (HCl salt, m. 187-9°); 2-oxo-3-ethyl-9,10-diethoxybenzo[a]quinolizine, m. 116-18°; 2-oxo-3-tetrahydrofurfuryl-9,10-dimethoxybenzo[a]quinolizine, m. 102-4° (HBr salt, m. 194-5°).

- IT 117866-98-5, Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolyl]methyl]-, 1-ethyl di-Me ester (preparation of)
 RN 117866-98-5 CAPLUS
 CN Malonic acid, benzyl[[1-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)isoquinolyl]methyl]-, 1-ethyl dimethyl ester (6CI) (CA INDEX NAME)



L5 ANSWER 79 OF 79 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1956:8410 CAPLUS

DN 50:8410

OREF 50:1705b-i,1706a-i,1707a-d

TI Podophyllotoxin and picropodophyllin. II. The synthesis of an open-chain analog

AU Drake, Nathan L.; Tuemmler, William B.

CS Univ. of Maryland, College Park

SO Journal of the American Chemical Society (1955), 77, 1204-9

CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA Unavailable

AB cf. C.A. 45, 6616g. The synthesis of α -(3,4,5-trimethoxybenzyl)- β -(α -hydroxy-3,4-methylenedioxybenzyl)butyrolactone (I), an open-chain analog of podophyllotoxin, is described. In addition, the stripped, open-chain analog, α -benzyl- β -(α -hydroxybenzyl)butyrolactone (II) is reported. 3,4,5-(MeO)₃C₆H₂CO₂H (III) esterified with EtOH and p-MeC₆H₄SO₃H as the catalyst gave 95% Et ester (IV), m. 52.5-4.5° (all m.ps. are corrected). IV (24.0 g.) in 50 cc. THF added during 20 min. to 50 cc. 2.1M LiAlH₄ in THF under N, the mixture ~~refluxed gently 2 h., cooled, treated cautiously with H₂O and then 10% H₂SO₄, the aqueous layer extracted with Et₂O, and the combined organic layer and Et₂O~~ extract washed with 5% aqueous NaHCO₃, dried, and distilled yielded 15.6 g. 3,4,5-(MeO)₃C₆H₂CH₂OH (V), viscous oil, b_{0.03} 115-20°. III (25.2 g.) and 5.0 g. LiAlH₄ refluxed 21 h. in 185 cc. THF, and the mixture worked up in the usual manner yielded 13.7 g. V, b_{0.02} 115-20°, n_D²⁵ 1.5431. V (15.6 g.) and 9.7 g. PhNMe₂ in 100 cc. dry C₆H₆ slowly treated with 9.4 g. pure SOCl₂ in 25 cc. C₆H₆, the mixture warmed to room temperature, refluxed 1 h., cooled, and treated with 30 cc. 1:5 HCl, the organic layer freed of acid and concentrated, and the residue distilled yielded 15.0 g. 3,4,5-(MeO)₃C₆H₂CH₂Cl (VI), b_{0.1} 110°, m. 58-61°; the distillate recrystd. from petr. ether gave 12.9 g. white crystals, m.

60-2°. NaH (15.4 g.) in 550 cc. CH₂(CO₂Et)₂ treated during 1 h. with 131 g. VI in 350 cc. CH₂(CO₂Et)₂, the mixture heated 20 h. at 105-10°, cooled, treated with a few drops AcOH and 50 cc. H₂O, the amber solution decanted from the coagulated salt, the excess CH₂(CO₂Et)₂ removed, and the residue recrystd. from 2.5 l. petr. ether yielded 172.5 g. 3,4,5-(MeO)3C₆H₂CH₂CH(CO₂Et)₂ (VII), white needles, m. 78-9°. 3,4,5-(MeO)3C₆H₂CHO (VIII) (0.75 g.), m. 73.8-5.0°, 0.63 g. CH₂(CO₂Et)₂, 0.45 g. AmCO₂H, and 0.15 g. piperidine in 35 cc. C₆H₆ refluxed under a Dean-Stark trap, the solution washed with H₂O and 5% aqueous NaHCO₃ and evaporated, and the residue recrystd. from 25 cc. petr. ether yielded 0.95 g. 3,4,5-(MeO)3C₆H₂CH:C(CO₂Et)₂ (IX), m. 69.2-70.4° (from petr. ether). Approx. 50% of a sample of IX which had stood 20 mo at room temperature no longer dissolved in boiling petr. ether; this material recrystd. from C₆H₆-petr. ether gave a dimer, m. 212-13°, probably 1,3-bis-(3,4,5-trimethoxyphenyl)-2,2,4,4-tetracarboethoxycyclobutane. IX hydrogenated over PtO₂ gave VII. VI (155 g.) gave by the method of Walker and Hauser (C.A. 40, 5712.1) with EtOMgCH(CO₂Et)₂ 217 g. 3,4,5-(MeO)3C₆H₂COCH(CO₂Et)₂ (X), white solid, m. 90.5-1.5° (from 1.2 l. 50% aqueous EtOH). X (4.5 g.) and 2.0 g. 10% Pd-C in 100 cc. absolute EtOH hydrogenated at room temperature and 2.5 atmospheric and the crude product recrystd. from 50 cc. petr. ether gave 2.4 g. VIII, m. 73.4-4.0°. X hydrogenated over PtO₂ gave 59% CH₂(CO₂Et)₂ and 68% V. V (1.0 g.) in 20 cc. 10% H₂SO₄ boiled 3 h., the mixture extracted with Et₂O, the extract filtered and evaporated slowly, and the small amount crystalline residue recrystd. from EtOH yielded 20 mg. 1,2,3,5,6,7-hexamethoxy-9,10-dihydroanthracene, m. 201.5-203°. 3,4-CH₂O₂C₆H₃CO₂H (XI) (113.5 g.), m. 230-2°, and 123 cc. pure SOCl₂ refluxed 5 h., the excess SOCl₂ removed, and the residue distilled gave 124 g. 3,4-CH₂O₂C₆H₃COCl (XII), b0.02 92°, m. 78-83°. When XII was prepared by the method of Bruchhausen and Gerhard (C.A. 33, 5391.4) with C₆H₆ as a diluent a considerable amount of anhydride of XI, m. 152.6-4.2°, was obtained, which boiled with 107% NaOH was hydrolyzed to XI, m. 231-3°. EtOMgCH(CO₂Et)₂ (XIII) (0.85 mol) in Et₂O refluxed 0.5 h. with 139 g. XII in 1 l. Et₂O, the mixture cooled, acidified with 10% H₂SO₄, and allowed to stand overnight, and the resulting deposit of large white crystals recrystd. from EtOAc-petr. ether gave 3,4-CH₂O₂C₆H₃COCH(CO₂Et)₂ (XIV), m. 69.5-71.0°. The crude XIV obtained by the evaporation of the Et₂O solution boiled 5 h. with 210 cc. AcOH, 140 cc. H₂O, and 27 cc. H₂SO₄, the orange-red solution made alkaline with 40% aqueous NaOH and extracted with Et₂O, the extract washed, dried, and evaporated, and the residue recrystd. from 3 l. petr. ether gave 97 g. 3,4-CH₂O₂C₆H₃Ac (XV), pale yellow solid, m. 84-7°; the aqueous solution acidified yielded 6.4 g. XI, m. 230°. XV (49.2 g.) in 1.5 l. dry Et₂O treated with 48 g. Br during 40 min., the Et₂O evaporated in vacuo, the brick-red residue treated with 500 cc. H₂O, washed with more H₂O, and recrystd. from 4 l. petr. ether with C gave 56 g. α-Br derivative (XVI), white plates, m. 90-2.5°. XIII (0.11 mol) in Et₂O treated with 19.9 g. BzCH₂Br in dry Et₂O, the mixture refluxed 1.5 h., cooled, and acidified with 75 cc. 10% H₂SO₄, the Et₂O solution evaporated, and the residual oil allowed to stand deposited 3 g. BzCH₂CH(CO₂Et)₂ (XVII), m. 120-1.2°; distillation of the remaining oil gave 8.2 g. CH₂(CO₂Et)₂, 3.1 g. BzCH₂Br, and 9.1 g. XVII. Mg (2.43 g.), 2.5 cc. absolute EtOH, and 0.25 cc. CCl₄ treated with 25.0 g. PhCH₂CH(CO₂Et)₂, b0.03 100°, n_D22 1.4862, in 10 cc. absolute EtOH, the

mixture refluxed 1.5 h., the clear solution treated with 150 cc. dry C₆H₆, the excess EtOH removed as an azeotrope with C₆H₆, the residual mixture treated with 19.9 g. BzCH₂Br in 125 cc. C₆H₆, the amber solution allowed to stand 7 days at room temperature and acidified with 75 cc. 10% H₂SO₄, the C₆H₆ layer evaporated, and the residue recrystd. from 400 cc. petr. ether gave 29.8 g. BzCH₂(PhCH₂)C(CO₂Et)₂ (XVIIa), white crystals, m. 75-7°.

3,4,5-(MeO)3C₆H₂CH₂(EtOMg)C(CO₂Et)₂ (0.23 mol) in C₆H₆ (prepared from VII) treated with 56 g. XVI in 1 l. C₆H₆, the mixture kept 7 days at room

temperature,

the yellow-green solution acidified with 100 cc. 10% H₂SO₄, washed with base, and evaporated, and the residue recrystd. twice from 50% aqueous EtOH yielded

88

g. di-Et ester (XVIII), white, m. 104-5°, of 3,4,5-

(MeO)3C₆H₂CH₂(3,4-CH₂O2C₆H₃COCH₂)C(CO₂H)₂ (XIX), 2,4-

dinitrophenylhydrazone, m. 172.5-4.0°. XVIII (1.0 g.) in 50 cc.

EtOH hydrogenated at room temperature and atmospheric pressure over 1.0 g. 10%

Pd-C and

the resulting crude product recrystd. twice from EtOH gave 0.3 g.

α-CO₂Et derivative (XX) of α-(3,4,5-trimethoxybenzyl)-γ-(3,

4-methylenedioxyphenyl)butyrolactone (XXI), m. 149.5-51.0°. XVIIa

(56.8 g.) in 150 cc. warm absolute EtOH added to 200 g. KOH in 600 cc. absolute EtOH, the mixture cooled, the deposit washed with small portions cold absolute

EtOH and then dry Et₂O, and dissolved in 400 cc. H₂O, and the solution

acidified with HCl yielded PhCH₂C(CH₂Bz)(CO₂H)₂ (XXII), m. 168-70°.

XVIII (33.8 g.) in 200 cc. warm absolute EtOH added to 175 g. KOH in 600 cc.

absolute EtOH, the mixture kept 0.5 h. at room temperature, chilled, and

filtered, the

filter residue washed with EtOH and Et₂O and dissolved in H₂O, and the

solution acidified gave XIX.2H₂O, m. 132-3° (decomposition) (from

EtOAc-petr. ether). Crude moist XXII from 56.8 g. XVIIa decarboxylated

thermally and the residue recrystd. from 400 cc. AcOH and 250 cc. H₂O

yielded 35 g. PhCH₂CH(CH₂Bz)CO₂H (XXIII), m. 173-4.5°; Me ester,

82%, m. 68.2-9.0°. Crude moist XIX.2H₂O thermally decomposed at

150° and the resulting yellow glass crystallized from EtOAc-petr. ether

with C yielded 22.8 g. 3,4,5-(MeO)3C₆H₂CH₂(3,4-CH₂O2C₆H₃COCH₂)CHCO₂H

(XXIV), m. 133.8-5.4°. XXIV dissolved in MeOH containing dry HCl

yielded 68% Me ester, m. 91-2.5° (from EtOAc-petr. ether). XXIV in

EtOH containing dry HCl kept 18 h. at room temperature gave the Et ester, m.

117-18° (from EtOH); 2,4-dinitrophenylhydrazone, m. 144-5°

(from EtOH). XXIV (3.1 g.) treated 24 h. at room temperature with 1.0 g.

NaBH₄,

the mixture acidified and extracted with Et₂O, the extract reextd. with

aqueous NaHCO₃,

and the solid from the NaHCO₃-extract (after treatment with EtOH) recrystd.

twice from aqueous EtOH gave 0.9 g. XXI, m. 95.5-7.5°. XXIII (7.12 g.)

in 31.7 cc. 0.926N NaOH treated with 2.40 cc. 37% aqueous CH₂O, the mixture

kept

48 h. at room temperature and acidified with dilute HCl, the precipitated gum

dissolved

in C₆H₆ and chromatographed on silicic acid, the column eluted with C₆H₆,

the resulting noncryst. product seeded and triturated with C₆H₆-petr.

ether, and the granular residue recrystd. from C₆H₆-petr. ether yielded

2.40 g. α-benzyl-β-benzoylbutyrolactone (XXV), white solid, m.

108-10°; 2,4-dinitrophenylhydrazone, m. 197-9°. In a

similar run with 12 equivs. CH₂O chromatog. on silicic acid yielded

approx. equal amts. XXV and 3-benzoyl-4-benzyl-4-hydroxy-3-hydroxymethyl-

γ-butyrolactone (XXVI) (which did not form a

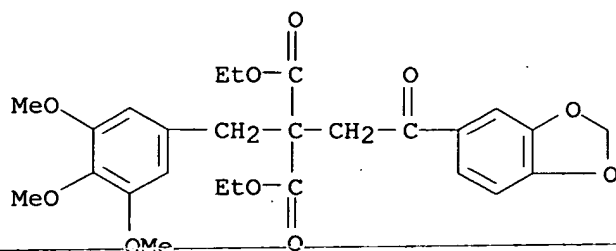
dinitrophenylhydrazone). XXIV (16.1 g.) in 48 cc. 0.926N NaOH kept 44 h.

at room temperature with 4.5 cc. 37% aqueous CH₂O, the mixture chilled and acidified, the gummy precipitate washed with H₂O and triturated several times with Et₂O, and the product (10.9 g.) recrystd. from EtOAc-petr. ether gave pure γ -HO derivative (XXVII) of α -(3,4,5-trimethoxybenzyl)- β -(3,4-methylenedioxybenzoyl)butyric acid (XXVIII), m. 135-7° (decomposition). XXVII heated at 150° until the sample was completely melted and the glassy product crystallized from EtOH gave the lactone of XXVII, m. 140.4-3.0°. XXVII lactone treated in warm EtOH with excess 0.1N NaOH, the mixture kept 0.5 h. at room temperature and back-titrated gave the saponification equivalent; if the mixture was boiled variable, low values were obtained depending upon the duration of the boiling. The lactone gave a yellow precipitate with 2,4-(O₂N)₂C₆H₃NHNH₂, but the product did not have a sharp m.p. XXV (2.38 g.) in 50 cc. EtOH hydrogenated 20 min. at room temperature and atmospheric pressure over 0.5 g. 10% Pd-C, the mixture filtered and evaporated, and the white solid residue (1.18 g.) recrystd. from 5 cc. EtOH gave 1.01 g. II, m. 149-60° (from C₆H₆-petr. ether); it was also prepared by the Pd-catalyzed hydrogenation of XXV in cyclohexane. XXV (3.9 g.) (noncryst. material) in EtOH hydrogenated 6 h. over Pd-C yielded 1.11 g. isomer of II, m. 103-3.6° (from C₆H₆-petr. ether). XXVII lactone (4.14 g.) hydrogenated 3.5 h. in 50 cc. EtOH over 1.3 g. 10% Pd-C the glassy product (3.5 g.) in 45 cc. EtOAc and 60 cc. petr. ether seeded and kept several days at -20° yielded 2.53 g. white powder which recrystd. twice gave 1.87 g. I, m. 104-8°. The noncryst. fraction from the reaction of IV with CH₂O yielded about 13% XXVIII, m. 166-7°.

IT 7400-87-5, Malonic acid, (3,4-methylenedioxyphenacyl) (3,4,5-trimethoxybenzyl)-, diethyl ester
(preparation of)

RN 7400-87-5 CAPLUS

CN Malonic acid, [3,4-(methylenedioxy)phenacyl] (3,4,5-trimethoxybenzyl)-, diethyl ester (8CI) (CA INDEX NAME)



=> s 14 not 15

L6 17 L4 NOT L5

=> dis 16 bib abs

L6 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:547244 CAPLUS

DN 141:225396

TI Novel nucleophilic C-C bond-forming tele-reaction of imidazole ring

AU Ohta, Shunsaku; Sato, Kentaro; Kawasaki, Ikuo; Yamaguchi, Yuko; Nishio, Satoko; Yamashita, Masayuki
 CS Kyoto Pharmaceutical University, Kyoto, 607-8414, Japan
 SO Journal of Heterocyclic Chemistry (2004); 41(3), 335-341
 CODEN: JHTCAD; ISSN: 0022-152X
 PB HeteroCorporation
 DT Journal
 LA English
 OS CASREACT 141:225396
 AB Reaction of 2-(1-chloro-2,2-dimethylpropyl)-1-methyl-1H-imidazole with di-Et methylmalonate in the presence of NaH gave a normal SN product, 2-[(1,1-diethoxycarbonylethyl)-2,2-dimethylpropyl]-1-methyl-1H-imidazole and two tele-reaction products, 5-(1,1-diethoxycarbonylethyl)-1-methyl-2-(2,2-dimethylpropyl)-1H-imidazole and trans-4,5-di-(1,1-diethoxycarbonylethyl)-4,5-dihydro-1-methyl-2-(2,2-dimethylpropyl)-1H-imidazole in 5, 17 and 70 % yields, resp. The scope and mechanism of this reaction are discussed.
 RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis 16 2-17 bib abs

L6 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:389622 CAPLUS
 DN 140:400059
 TI Composition containing activators of IC potassium channels and calcineurin antagonists and their use for the treatment of inflammatory diseases
 IN Kaesler, Susanne; Koegel, Heidi; Alzheimer, Christian; Sych, Michael
 PA Switch Biotech A.-G., Germany; Ludwig-Maximilians-Universitat; ETH Zurich
 SO Ger. Offen., 73 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|------------------|----------|
| PI | DE 10250870 | A1 | 20040513 | DE 2002-10250870 | 20021031 |
| | WO 2004039409 | A2 | 20040513 | WO 2003-EP12130 | 20031031 |
| | WO 2004039409 | A3 | 20040910 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | DE 2002-10250870 | A | 20021031 | | |

OS MARPAT 140:400059
 AB The invention discloses compns., containing activators of IC (intermediate conductance) potassium channels and calcineurin antagonists, as well as their use for the treatment of inflammatory diseases, in particular inflammatory skin diseases.

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:356066 CAPLUS
 DN 141:71518
 TI Synthesis of original benzo[g]quinoxaline-5,10-diones by bis-SRN1 methodology
 AU Remusat, Vincent; Terme, Thierry; Gellis, Armand; Rathelot, Pascal; Vanelle, Patrice
 CS Laboratoire de Chimie Organique Pharmaceutique LCOP, UMR CNRS 6517, Faculte de Pharmacie, Universite de la Mediterranee, Marseille, 13385, Fr.
 SO Journal of Heterocyclic Chemistry (2004), 41(2), 221-225
 CODEN: JHTCAD; ISSN: 0022-152X
 PB HeteroCorporation
 DT Journal
 LA English
 OS CASREACT 141:71518
 AB A new heterocyclic bioreductive bis-alkylating agent, 2,3-bis(chloromethyl)benzo[g]quinoxaline-5,10-dione, was prepared in a four-steps synthesis. It was shown to react under electron transfer conditions with 2-nitropropane anion by an bis-SRN1 mechanism to give three C-alkylation products in excellent yields. Extension of this bis-SRN1 reaction to various nitronate or malonate anions and S-centered anions led to a new class of potentially active benzo[g]quinoxaline-5,10-dione derivs.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

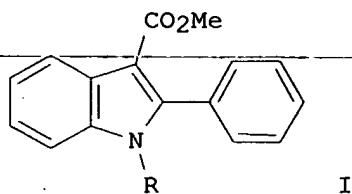
L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:306980 CAPLUS
 DN 141:33320
 TI Design, synthesis and biological activity of amidinobicyclic compounds (derivatives of DX-9065a) as factor Xa inhibitors: SAR study of S1 and aryl binding sites
 AU Komoriya, Satoshi; Kanaya, Naoaki; Nagahara, Takayasu; Yokoyama, Asako; Inamura, Kazue; Yokoyama, Yukio; Katakura, Shin-ichi; Hara, Tsuyoshi
 CS Tokyo R&D Center, Daiichi Pharmaceutical Co. Ltd, Edogawa-ku, Tokyo, 134-8630, Japan
 SO Bioorganic & Medicinal Chemistry (2004), 12(9), 2099-2114
 CODEN: BMECEP; ISSN: 0968-0896
 PB Elsevier Ltd.
 DT Journal
 LA English
 OS CASREACT 141:33320
 AB Since factor Xa (fXa) plays a pivotal role in the blood coagulation cascade, inhibition of fXa is thought to be an effective treatment for a variety of thrombotic events. (2S)-2-[4-[[[(3S)-1-Acetimidoyl-3-pyrrolidinyl]oxy]phenyl]-3-(7-amidino-2-naphthyl)propanoic acid hydrochloride pentahydrate (DX-9065a) was previously found in our laboratory as a novel orally active factor Xa inhibitor. DX-9065a exhibits a strong inhibitory activity toward fXa by occupying the substrate recognition (called S1) sites and aryl binding sites of fXa. Herein we describe conversions of the amidinonaphthalene and the acetimidoylpyrrolidine moieties of DX-9065a. Some compds. showed remarkably increased in vitro anti-factor Xa and PRCT activities compared with those of DX-9065a. The most promising compound 38 showed four times the prolongation of APTT against DX-9065a after oral administration to rats.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:814483 CAPLUS
 DN 140:263036
 TI A New Double-Decker Lu(III) Diphthalocyanine with Eight Peripheral Benzo-15-crown-5 Units
 AU Kocak, M. Burkut; Cihan, Ali; Guersoy, Sueleyman; Okur, A. Ihsan; Guel, Ahmet; Bekaroglu, Oezer
 CS Department of Chemistry, Technical University of Istanbul, Istanbul, Turk.
 SO Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry (2003), 33(9), 1527-1533
 CODEN: SRIMCN; ISSN: 0094-5714
 PB Marcel Dekker, Inc.
 DT Journal
 LA English
 AB The authors describe a lutetium(III) bis(phthalocyaninate) complex which contains eight (benzo-15-crown-5)bis(ethoxycarbonyl)oxopropyl units. The starting compound was di-Et (3,4-dicyanophenyl)acetoxymalonate (1). The synthesis of the desired compound was accomplished by the reaction of 1 with lutetium acetate in hexanol in the presence of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) as a strong base. The ESR spectrum confirmed the radical nature of the complex.
 RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:644244 CAPLUS
 DN 139:307656
 TI A direct entry to the 1-methoxyindole skeleton and to the corresponding indoles by a novel rearrangement: general syntheses of substituted 1-methoxyindoles
 AU Selvakumar, N.; Reddy, B. Yadi; Azhagan, A. Malar; Khera, Manoj Kumar; Babu, J. Moses; Iqbal, Javed
 CS Department of Discovery Chemistry, Discovery Research, Dr. Reddy's Laboratories Ltd., Hyderabad, 500 050, India
 SO Tetrahedron Letters (2003), 44(37), 7065-7069
 CODEN: TELEAY; ISSN: 0040-4039
 PB Elsevier Science B.V.
 DT Journal
 LA English
 OS CASREACT 139:307656
 GI

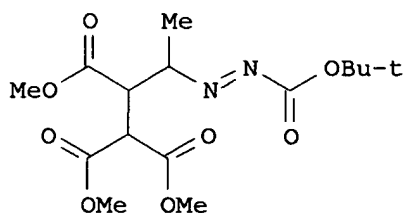


AB A short and efficient route to 1-methoxyindoles by a novel rearrangement is disclosed. This route involves only three steps from com. available nitro compds. The methodol. is also generalized with a variety of examples to afford a series of 2-substituted-1-methoxyindoles possessing an electron-withdrawing group at the 3-position. 1-Methoxyindole I (R = OMe) was converted to indole I (R = H) under mild conditions, thereby

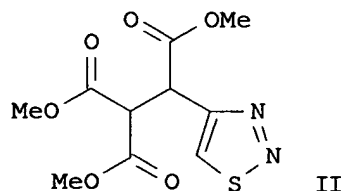
constituting a new synthesis of substituted indoles.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

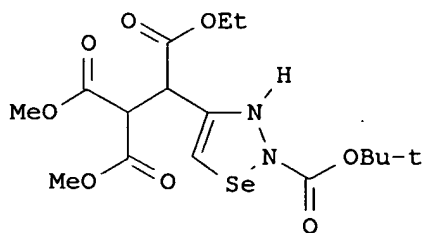
L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:93716 CAPLUS
DN 138:287593
TI Expeditionary synthesis of new 1,2,3-thiadiazoles and 1,2,3-selenadiazoles from 1,2-diaza-1,3-butadienes via Hurd-Mori-type reactions
AU Attanasi, Orazio A.; De Crescentini, Lucia; Favi, Gianfranco; Filippone, Paolino; Giorgi, Gianluca; Mantellini, Fabio; Santeusano, Stefania
CS Istituto di Chimica Organica, Universita degli Studi di Urbino, Urbino, 61029, Italy
SO Journal of Organic Chemistry (2003), 68(5), 1947-1953
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 138:287593
GI



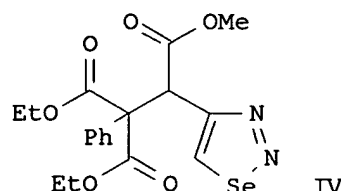
I



II



III



IV

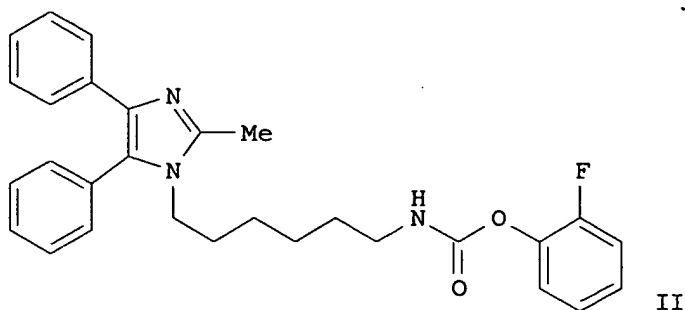
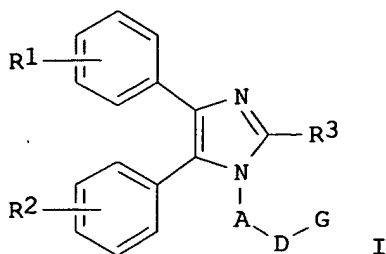
AB α -Substituted hydrazones, e.g. I, obtained from 1,2-diaza-1,3-butadienes and methylenic or methinic activated substrates gave rise to a wide range of cyclic compds. In particular, in the presence of thionyl chloride as solvent-reagent, they were transformed into 1,2,3-thiadiazoles, e.g. II, with selenium oxychloride into new 4-substituted-2,3-dihydro-1,2,3-selenadiazoles, e.g. III, while with selenium dioxide, they were transformed into 4-substituted-1,2,3-selenadiazoles, e.g. IV. We have also examined the nucleophilic behavior of 1,2,3-thiadiazole II in the reaction with 1,2-diaza-1,3-butadienes that produced, under basic conditions, 4-hydrazono-1-(1,2,3-thiadiazolyl)pentane derivs. This event represents an interesting example of stereoselective synthesis because it leads exclusively to the formation of the RR/SS racemic mixture. These latter compds., treated with thionyl chloride, gave the corresponding 1,3-di-1,2,3-thiadiazolylpropane derivs.,

while with sodium methoxide they afforded 1,2,3-thiadiazolyl-2-oxo-2,3-dihydro-1H-pyrrole systems.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:849426 CAPLUS
DN 137:353021
TI Preparation of bisarylimidazolyl fatty acid amide hydrolase inhibitors for treatment of pain
IN Sit, Sing-Yuen; Xie, Kai
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2002087569 | A1 | 20021107 | WO 2002-US12853 | 20020423 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2002188009 | A1 | 20021212 | US 2002-128480 | 20020423 |
| | US 6562846 | B2 | 20030513 | | |
| | EP 1389107 | A1 | 20040218 | EP 2002-728952 | 20020423 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2004532229 | T2 | 20041021 | JP 2002-584915 | 20020423 |
| PRAI | US 2001-286827P | P | 20010427 | | |
| | WO 2002-US12853 | W | 20020423 | | |
| OS | MARPAT 137:353021 | | | | |
| GI | | | | | |



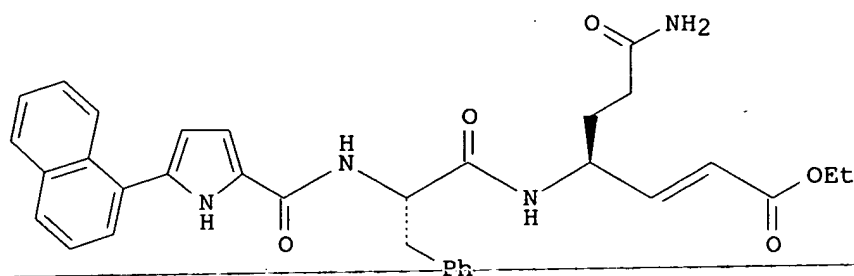
AB Title compds. I [wherein R1 and R2 = independently H, alkyl, or halo; R3 = (cyclo)alkyl; A = alkylene or L; L = C6H4O-alkylene; D = CO₂, CONG₁, NHC0₂, or NHC0₂N:CG₁; G = H, haloalkyl, (cyclo)alkyl, pyridyl, or (un)substituted Ph or (CH₂)₁₋₂Ph; G₁ = H or (halo)alkyl; or AD is optionally interrupted with CHJ, ZC₆H₄, or Z(CH₂)₁₋₃; Z = O or S; J = alkyl or Ph; with provisos] were prepared as fatty acid amide hydrolase (FAAH) inhibitors. For example, cycloaddn. of benzil with AcONH₄ and MeCHO in glacial AcOH gave 2-methyl-4,5-diphenyl-1H-imidazole (29%). Alkylation with Et 7-bromoheptanoate in the presence of NaH in DMF (72%) followed by saponification with NaOH in EtOH afforded 7-(2-methyl-4,5-diphenylimidazol-1-yl)heptanoic acid. Stepwise addition of the azide, N₃PO(OPh)₂, and 2-FC₆H₄OH to a suspension of the heptanoic acid in TEA and toluene produced the carbamate II (55%). The latter inhibited recombinant human FAAH with IC₅₀ < 10 nM. In addition, II gave results similar to known analgesics in the in vivo rat formalin test (acute and chronic chemo-induced pain assay), the Hargreaves test (acute thermal pain assay), and the Chung model (neuropathic pain assay). Thus, I and their pharmaceutical compns. are useful for the treatment of pain, particularly neuropathic pain, psychomotor disorder, hypertension, cardiovascular disease, eating disorder, nausea, AIDS-related complex, glaucoma, inflammation, psoriasis or multiple sclerosis, and other conditions the treatment of which can be effected by inhibiting FAAH.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:780850 CAPLUS
DN 135:331676
TI Preparation of pyrrole-containing peptidomimetic compounds as antipicornaviral agents
IN Johnson, Theodore O., Jr.; Hua, Ye; Luu, Hiep T.; Dragovich, Peter S.
PA Agouron Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 206 pp.

CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|------|-------------------|------|----------|--|----------|--|
| PI | WO 2001079167 | A2 | 20011025 | WO 2001-US12333 | 20010412 | |
| | WO 2001079167 | A3 | 20020228 | | | |
| | W: | | | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | |
| | RW: | | | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | |
| | CA 2406475 | AA | 20011025 | CA 2001-2406475 | 20010412 | |
| | US 2002006943 | A1 | 20020117 | US 2001-834783 | 20010412 | |
| | US 6610730 | B2 | 20030826 | | | |
| | EP 1274682 | A2 | 20030115 | EP 2001-925037 | 20010412 | |
| | R: | | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | |
| | BR 2001010077 | A | 20030617 | BR 2001-10077 | 20010412 | |
| | JP 2003531139 | T2 | 20031021 | JP 2001-576769 | 20010412 | |
| | ZA 2002008257 | A | 20030725 | ZA 2002-8257 | 20021014 | |
| | US 2003225042 | A1 | 20031204 | US 2003-435082 | 20030512 | |
| PRAI | US 2000-197796P | P | 20000414 | | | |
| | US 2000-198497P | P | 20000418 | | | |
| | US 2001-834783 | A3 | 20010412 | | | |
| | WO 2001-US12333 | W | 20010412 | | | |
| OS | MARPAT 135:331676 | | | | | |
| GI | | | | | | |



AB Peptidomimetic compds. RaCON(Rb)CHRCrCd:CZZ1 [Ra is alkyl-, cycloalkyl-, aryl- or heteroarylcarbonylalkyl, alkyl-, cycloalkyl-, heterocycloalkyl-, aryl- or heteroarylcarbonylaminoalkyl or -aminocarbonylalkyl, where each alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl may be substituted; Rb is H or (un)substituted alkyl; Rd is H, halo, OH, (un)substituted alkyl, alkoxy or alkylthio; Rc is CReRf-Al(R)-CO-A4-(A3)p-R, where R2 = (A2)m (m = 0 or 1; R = H for m = 0); Re, Rf = H, alkyl; p = 0-5; A1 = CH or N; A2 = CRgRhRi, NRgRi, SRg, S(O)Rg, SO2Rg, O(Rg) (Rg, Rh, Ri = H or alkyl); A3 = CRgRh, NRi, S, SO, SO2, O; A4 = NRjRk, CRgRhRi, O(Rk) (Rk = H or alkyl); Z, Z1 = H, F (un)substituted alkyl, cycloalkyl,

heterocycloalkyl, aryl or heteroaryl or CZZ1 is (hetero)cycloalkyl (with provisos)] were prepared for inhibiting or blocking the biol. activity of the picornaviral 3C protease. Thus, compound I was prepared by coupling 5-(1-naphthyl)-1H-pyrrole-2-carboxylic acid chloride (preparation given) with Phe-Gln-resin and showed Kobs/I = 30,800 M⁻¹s⁻¹ for inhibition of Rhinovirus 3C virus, EC50 = 0.109 μ M in the antioxsackieviral cell culture assay, and CC50 (50% cytotoxic dose) >10 μ M.

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:303088 CAPLUS

DN 135:122446

TI Straightforward entry to new 4-substituted 1,2,3-thiadiazoles from 1,2-diaza-1,3-butadienes via Hurd-Mori reaction

AU Attanasi, Orazio A.; De Crescentini, Lucia; Filippone, Paolino; Mantellini, Fabio

CS Istituto di Chimica Organica, Universita di Urbino, Urbino, 61029, Italy

SO Synlett (2001), (4), 557-559

CODEN: SYNLES; ISSN: 0936-5214

PB Georg Thieme Verlag

DT Journal

LA English

OS CASREACT 135:122446

AB 1-(Tert-butoxycarbonyl)-1,2-diaza-1,3-butadienes react with activated methylenic and methinic compds. to yield α -substituted hydrazones, which, in the presence of SOCl₂ as solvent-reactant, led to 1,2,3-thiadiazoles via Hurd-Mori cyclocondensation.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:162869 CAPLUS

DN 134:347956

TI Design, syntheses, and structure-activity relationships of indan derivatives as endothelin antagonists; new lead generation of non-peptidic antagonist from peptidic leads

AU Morimoto, H.; Fukushima, C.; Yamauchi, R.; Hosino, T.; Kikkawa, K.; Yasuda, K.; Yamada, K.

CS Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd, Toda-shi, Saitama, 335-8505, Japan

SO Bioorganic & Medicinal Chemistry (2001), 9(2), 255-268

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

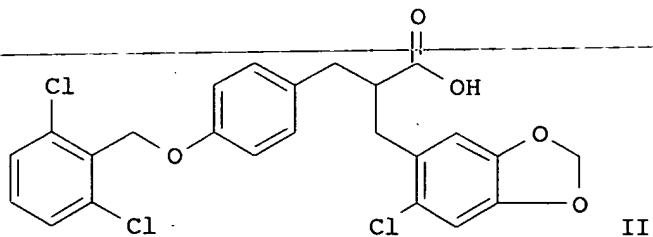
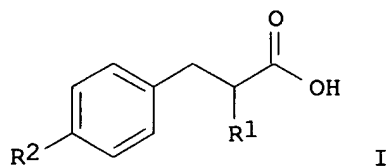
OS CASREACT 134:347956

AB A new lead generation of non-peptidic ETA antagonists from two peptidic ETA-selective ones, BQ-123 and FR139317, was performed. Using computer assisted mol. modeling, a putative pharmacophore was constructed from the superposition of the reported three-dimensional structure of the cyclic peptide BQ-123 and a presumable β -turn active conformation of the linear peptide FR139317 formed by an intramol. hydrogen bond. According to this model, a new series of indan derivs. were designed and synthesized. Among these, 5-isobutyrylamino-6-(1-naphthylmethoxy)-3-(2-thienyl)-1-indancarboxylic acid showed a moderate ETA antagonistic activity (IC₅₀=28 μ M).

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2001:152668 CAPLUS
 DN 134:193420
 TI Preparation of benzenepropanoic acid derivatives as fatty acid synthase inhibitors
 IN Christensen, Siegfried B., IV; Daines, Robert A.; Leber, Jack D.; Weinstock, Joseph
 PA Smithkline Beecham Corporation, USA
 SO PCT Int. Appl., 20 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2001014362 | A1 | 20010301 | WO 2000-US23073 | 20000823 |
| | W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1206463 | A1 | 20020522 | EP 2000-957681 | 20000823 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| | JP 2003507467 | T2 | 20030225 | JP 2001-518449 | 20000823 |
| PRAI | US 1999-150276P | P | 19990823 | | |
| | WO 2000-US23073 | W | 20000823 | | |
| OS | MARPAT 134:193420 | | | | |
| GI | | | | | |



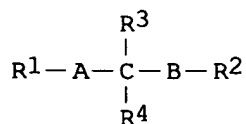
AB Title compds. (I) [wherein R1 = alkyl, (hetero)arylalkyl, heteroaryl, or (alkyl)cycloalkyl; R2 = O(CH2)mAr, NR3(CH2)mAr, NR4COAr, or NR4SO2Ar; R3 = H, alkyl(aryl), acyl, COAr; R4 = H or alkyl(aryl); Ar = (hetero)aryl; m = 0-3] were prepared as inhibitors of the fatty acid synthase, 3-ketoacyl-ACP

synthase (Fab H), for use as a new class of antibiotics. For example, the α -piperonylbenzenepropanoic acid (II) was formed by coupling 4-(2,6-dichlorobenzoyloxy)benzaldehyde (preparation given) with di-Et malonate in the presence of piperidine and glacial AcOH in benzene (97%), reduction using NaBH₄ in EtOH (88%), alkylation with 6-chloropiperonyl chloride in DMF (85%), and deesterification using KOH in EtOH (100%). I are active against a wide range of organisms, including both Gram-neg. organisms, e.g. *Escherichia coli* and *Klebsiella pneumoniae*, and Gram-pos. organisms, e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, and *Enterococcus faecium*, including isolates resistant to existing antibiotics (no data).

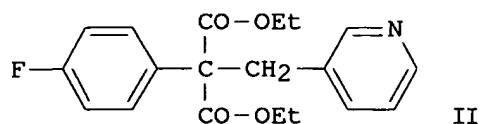
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:441757 CAPLUS
DN 133:73936
TI Preparation of substituted malonic acid esters as ion channel activating agents
IN Beyer, Jurgen; Jensen, Bo Skaaning; Strobaek, Dorte; Christophersen, Palle; Teuber, Lene
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------------|--|----------|-----------------|----------|
| PI | WO 2000037422 | A2 | 20000629 | WO 1999-DK731 | 19991222 |
| | WO 2000037422 | A3 | 20000914 | | |
| | W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| | EP 1140784 | A2 | 20011010 | EP 1999-962125 | 19991222 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| | JP 2002533318 | T2 | 20021008 | JP 2000-589494 | 19991222 |
| | US 2002169203 | A1 | 20021114 | US 2001-854694 | 20010515 |
| PRAI | DK 1998-1722 | A | 19981222 | | |
| | DK 1999-403 | A | 19990323 | | |
| | DK 1999-660 | A | 19990512 | | |
| | WO 1999-DK731 | W | 19991222 | | |
| OS | MARPAT 133:73936 | | | | |
| GI | | | | | |



I



II

AB The invention relates to ion channel activating agents, specifically malonic acid esters (I) [wherein A and B = independently (CH₂)_n, (CH₂)_nY, Y(CH₂)_n, or (CH₂)_nY(CH₂)_m; m and n = independently 0-4; Y = O, S, or (alkyl)amino; R₁, R₂, R₃, and R₄ = independently (cyclo)alkyl, alkenyl, alkynyl, amino, trihalomethyl, NO₂, CN, Ph, alkoxy(alkyl), alkylthio(alkyl), acyl, amido, carboxy, (un)substituted heterocyclyl or aryl(alkyl), etc.; or R₃ and R₄ together = (un)substituted polycyclic or hetero(poly)cyclic group]. In particular, the compds. are useful as openers SKCa, IKCa, and BKCa channels. The invention also relates to the use of these SK/IK/BK channel-activating agents for the manufacture of medicaments, and to pharmaceutical compns. comprising them. The compds. are useful for the treatment or alleviation of a wide variety of diseases and conditions associated with SK/IK/BK channels, including respiratory diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhea, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophias, xerostomia, diabetes type II, hyperinsulinemia, premature labour, baldness, cancer, and immune suppression. In particular, the compds. are expected to be useful as immunosuppressants. For instance, addition of 3-picolyl chloride to di-Et 2-(4-fluorophenyl)malonate treated with NaH in DMF and heating to 80°C overnight gave II (22%). In an electrophysiol. experiment using cloned human placental intermediate-conductance Ca²⁺-activated K⁺ channels (IK channels), expressed in HEK293 cells, II and other invention compds. showed activity at concns. of $\leq 10 \mu\text{M}$, and are thus potent SK/IK/BK channel activating agents.

L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:286739 CAPLUS

DN 133:98612

TI Novel crown ether-substituted phthalocyanines

AU Kocak, Makbule; Cihan, Ali; Okur, Ali Ihsan; Gul, Ahmet; Bekaroglu, Ozer
CS Department of Chemistry, Technical University of Istanbul, Istanbul, 80626, Turk.

SO Dyes and Pigments (2000), 45(1), 9-14
CODEN: DYPIDX; ISSN: 0143-7208

PB Elsevier Science Ltd.

DT Journal

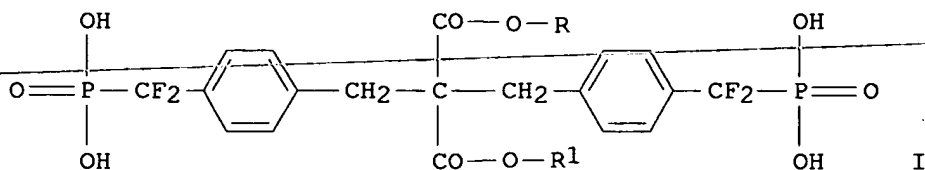
LA English

AB A novel macrocycle was synthesized from 4'-(α -bromoacetyl)benzo-15-crown-5, 4-nitrophthalonitrile and di-Et malonate; its cyclotetramerization gives Cu(II), Co(II) and Pd(II) phthalocyanines (Pcs) with four benzo-15-crown-5 substituents on the periphery. The effects of alkali metal cations with these Pcs was studied through the changes in the visible spectra. The newly synthesized compds. also were characterized by elemental analyses, IR, ¹H NMR.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:210184 CAPLUS
 DN 132:222660
 TI Phosphonic acid derivatives as inhibitors of PTP-1B
 IN Leblanc, Yves; Dufresne, Claude; Wang, Zhaoyin; Li, Chun Sing; Gauthier, Jacques Y.; Therien, Michel; Lau, Cheuk K.; Roy, Patrick
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 137 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2000017211 | A1 | 20000330 | WO 1999-CA864 | 19990921 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 6174874 | B1 | 20010116 | US 1999-398356 | 19990917 |
| | CA 2344927 | AA | 20000330 | CA 1999-2344927 | 19990921 |
| | AU 9957241 | A1 | 20000410 | AU 1999-57241 | 19990921 |
| | AU 761596 | B2 | 20030605 | | |
| | EP 1115729 | A1 | 20010718 | EP 1999-944200 | 19990921 |
| | EP 1115729 | B1 | 20030219 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | AT 232873 | E | 20030315 | AT 1999-944200 | 19990921 |
| | ES 2192396 | T3 | 20031001 | ES 1999-944200 | 19990921 |
| PRAI | US 1998-101164P | P | 19980921 | | |
| | US 1999-127420P | P | 19990401 | | |
| | WO 1999-CA864 | W | 19990921 | | |
| OS | MARPAT 132:222660 | | | | |
| GI | | | | | |



AB Anti-diabetic and anti-obesity title compds. such as malonates I (R = R1 = benzyl, I-Pr, H; R = Me, R1 = benzyl, H) were prepared by several standard methods. Among the approx. 50 compds. prepared were (4-{3-(benzyloxy)-2-(benzyloxycarbonyl)-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-oxopropyl}phenyl)difluoromethylphosphonic acid, (4-{3-(benzyloxy)-2-(benzyloxycarbonyl)-2-[4-(1,2,3-thiadiazol-4-yl)benzyl]-3-

oxopropyl}phenyl)difluoromethylphosphonic acid, bis{4-[difluoro(phosphono)methyl]benzyl}di-2-benzothiazolylmethane, and {4-[2-benzotriazol-1-yl-3-(4-bromophenyl)-2-phenylpropyl]phenyl}difluoromethylphosphonic acid.

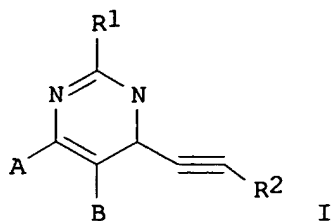
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:196451 CAPLUS
DN 133:26469
TI AMP Deaminase Inhibitors. 4. Further N3-Substituted Coformycin Aglycon
Analogues: N3-Alkylmalonates as Ribose 5'-Monophosphate Mimetics
AU Bookser, Brett C.; Kasibhatla, Srinivas Rao; Erion, Mark D.
CS Metabasis Therapeutics Inc., San Diego, CA, 92121, USA
SO Journal of Medicinal Chemistry (2000), 43(8), 1519-1524
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB AMP deaminase (AMPDA) inhibitors increase the levels of extracellular adenosine and preserve intracellular adenylate pools in cellular models of ATP depletion and therefore represent a potential new class of antiischemic drugs. Recently we reported that replacement of the ribose 5'-monophosphate component of the very potent transition-state analog AMPDA inhibitor coformycin monophosphate with a simple alkylcarboxy group resulted in potent, selective, and cell-penetrating AMPDA inhibitors. Here we report that replacement of this alkylcarboxy group with an α -substituted alkylmalonic acid resulted in enhanced inhibitor potency. The lead compound, 3-(5,5-dicarboxy-6-(3-(trifluoromethyl)phenyl)-n-hexyl)coformycin aglycon, exhibited an AMPDA K_i of 0.029 μ M which is (3 + 105)-fold lower than the K_M for the natural substrate AMP. A comparison of inhibitory potencies shows that the diacid analogs with α -benzyl substituents are 2-10-fold more inhibitory than similar monoacid-monoester, monoester-monoamide, or diester derivs. Finally, these diacid analogs are 2-40-fold more potent inhibitors than the corresponding monocarboxylates.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:206884 CAPLUS
DN 130:267450
TI Preparation of ethynylpyrimidine derivatives as tyrosine kinase inhibitors and their pharmaceutical uses
IN Kitano, Yasunori; Kawahara, Eiji; Takayanagi, Hisao; Suzuki, Takeshi; Ohya, Atsushi; Hara, Hiroto
PA ~~Mitsubishi Chemical Industries Ltd., Japan~~
SO ~~Jpn. Kokai Tokkyo Koho, 235 pp.~~
~~CODEN: JKXXAF~~
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|------|----------|-----------------|----------|
| PI | JP 11080131 | A2 | 19990326 | JP 1997-251348 | 19970901 |
| PRAI | JP 1997-251348 | | 19970901 | | |
| OS | MARPAT 130:267450 | | | | |
| GI | | | | | |



AB The derivs. I [A, B = NO₂, (CH₂)_n (n = 0, 1), NR₃R₄ (R₃, R₄ = H, C1-5 alkyl which may be substituted with CO₂H or C1-5 alkoxy carbonyl) or AB = CX₁:CX₂CX₃:CX₄ [X₁-X₄ = H, halo, NO₂, OR (R = C3-8 cycloalkyl which may contain O, C1-5 alkyl which may be substituted with C1-5 alkoxy, amino, morpholino), amino which may be substituted with C1-5 alkyl; neighboring 2 groups of X₁-X₄ may be bonded to each other to be C1-5 oxyalkylene], N: CX₅CX₆:CX₇ (X₅-X₇ = H, halo, C1-5 alkoxy, amino which may be substituted with C1-5 alkyl), CX₈:NCX₉:CX₁₀ (X₈-X₁₀ = any group given for X₅-X₇), N: CX₁₁CX₁₂:N (X₁₁, X₁₂ = H, C1-5 alkyl), W: CX₁₃NX₁₄ (W = N, CX₁₅, X₁₃-X₁₅ = H, C1-5 alkyl), CX₁₆:CX₁₇O (X₁₅, X₁₇ = H, C1-5 alkyl); R₁ = H, halo, (halo)phenyl, C1-5 (phenyl)alkyl, C1-5 alkoxy which may be substituted with CO₂H or C1-5 alkoxy carbonyl, OH, amino which may be substituted with C1-5 alkyl or C1-5 alkanoyl; R₂ = CR₃R₄R₅ [R₃, R₄ = H, halo, pyridyl, pyridazinyl, (C3-8 cycloalkyl)-C1-5 alkyl, etc.]; R₅ = OH, C1-5 alkyl, C1-5 alkoxy carbonyl, C1-5 alkanoyloxy, CO₂H, etc], their hydrates, pharmacol. acceptable salts, optically-active isomers, racemates, and diastereomer mixts. are prepared I are useful for prophylactic and/or therapeutic agents for diseases due to acceleration of tyrosine kinase activity, e.g. as antitumor agents, immunosuppressants, platelet aggregation inhibitors, antiatherosclerotics, inflammation inhibitors, etc. Et₂NCMe₂C.tplbond.CH was treated with EtMgBr and the resulting grignard reagent was treated with 4-chloro-2-phenylquinazoline (preparation given) to give I (R₁ = Ph, R₂ = CMe₂NEt₂, AB = CH:CHCH:CH) (II). This was dissolved in Et₂O and treated with HCl/EtOAc to give II.HCl. IC₅₀ values of this salt against EGF receptor tyrosine kinase activity and growth of human nasopharyngeal carcinoma KB cells were 14 μM and 0.89 μM, resp.

=> log y

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

438.55

600.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY

TOTAL
SESSION

CA SUBSCRIBER PRICE

-70.08

-70.08

STN INTERNATIONAL LOGOFF AT 14:47:34 ON 03 MAR 2005